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Basic Concepts

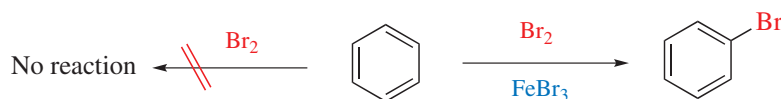
1.1 Introduction to Reaction Mechanisms

Chemical reactions are the processes by which chemicals interact to form new chemicals with different compositions. A new compound formed as a result of a chemical reaction does not bear the properties of the starting compounds; it has its own unique properties. In order for a chemical reaction to begin, some conditions (temperature, pressure, catalyst, etc.) must exist. For some compounds, it is sufficient to bring them together to start a chemical reaction. For example, water and sodium (provided they do not come in contact with air) are normally stable. However, a very violent reaction happens when these two come together. Sodium metal reacts rapidly with water to form a colorless solution of sodium hydroxide (NaOH) and releases hydrogen gas.



There is a common point regarding all chemical reactions, namely, transfer of electrons from one reactant to another (electron exchange). Therefore, one of the starting compounds should be capable of denoting electrons, while the other should accept electrons. In order for electron exchange to take place, some reactions require catalysts. A catalyst is a substance that can be added to a reaction to increase the reaction rate without being consumed in the process. The function of catalysts is to facilitate electron transfer by activating bond electrons and to lower activation energies (E_a). As a result of electron transfer, some bonds are broken, some bonds rearrange, and new bonds are formed.

Benzene is an unreactive compound in the presence of halogens (Cl_2 , Br_2 , or I_2) because they are not electrophilic enough to attack the benzene ring and disrupt its aromaticity. However, the halogens must be activated by Lewis acid catalysts such as FeBr_3 or AlBr_3 . FeBr_3 accepts electron pairs from bromine and makes it much more electrophilic. For a detailed mechanism, see Section 6.6.



Let us roughly analyze the processes that occur during the reaction of sodium with water. We see that the hydrogen atom, which is bonded to oxygen, breaks off from oxygen and forms hydrogen gas by binding to another hydrogen atom; on the other hand, the neutral sodium atom is oxidized by donating an electron and forming an ionic bond with the hydroxyl anion. This reaction appears to be very simple. However, complex processes are involved. We need to understand how products are formed as a result of a reaction. When a reactant turns into a product, we should look at which intermediates are involved during this reaction.

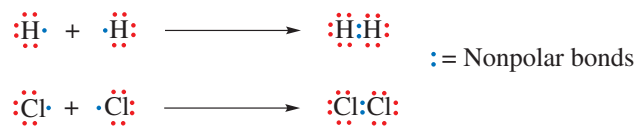
If we have a good understanding of what is going on at the intermediate stages, then we can guess what kind of products are formed as a result of the reaction. The step-by-step sequence of the intermediate stages of a reaction until the product is formed is called the *reaction mechanism*.

We have to understand what is happening at the intermediate levels. Otherwise, if we try to learn about a chemical reaction by writing reactants on one side of the equation and products on the other side, we will not be able to master organic chemistry. If the reaction mechanism is learned well, then one can see that organic chemistry is as enjoyable and systematic

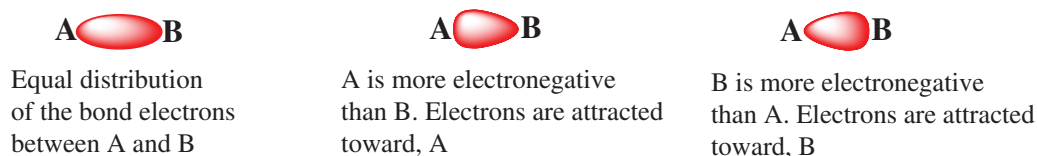
as mathematics. This is because, once the reaction mechanism is known, it is possible to predict what reaction will occur between two reactants and what products will be formed. Otherwise, if the reactions are learned without examining the mechanism (a type of learning based on memorizing), it becomes clear that organic chemistry cannot be understood. Then, organic chemistry becomes extremely boring.

Let us go back to the beginning. We emphasized that all chemical reactions occur as a result of electron exchange. To decide whether a compound is an electron donor or not, it is necessary to examine its electronic structure. In other words, it is necessary to examine the bonds between atoms and how the bonds are polarized.

The elements share electrons so that each atom attains a noble gas configuration. For example, two chlorine atoms can each attain a filled second shell by sharing their unpaired valence electrons. A bond formed by sharing electrons is called a *covalent bond*. Similarly, the hydrogen molecule, H_2 , can also form a covalent bond by sharing electrons. The atoms that share the bonding electrons in the $H-H$ and $Cl-Cl$ covalent bonds are identical. Such bonds are called nonpolar covalent bonds. In some compounds, the bonding electrons are shared equally between the atoms.



In contrast, the bonding electrons between two different atoms are more attracted to one atom than to another because of different electronegativities (the ability of an atom in a molecule to attract electrons toward itself). The symmetrical distribution of the electrons between the two atoms is disrupted. This condition is called *bond polarization*.

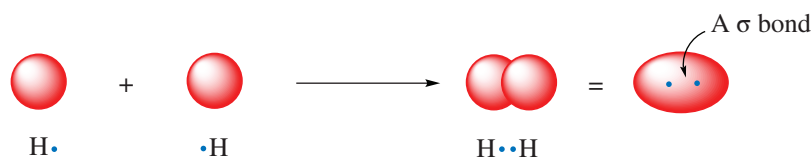


If electrons are attracted more strongly by A, the electron density increases around atom A and decreases around B. Therefore, this polarization makes A and B atoms more reactive. In such a case, groups with high electron density prefer to bind to atom B, while those with low electron density prefer to bind to atom A. In order to understand the reaction mechanism, electron polarization between bonds must be known very well. In this chapter, we first discuss about bonds, and in the next section, we focus on bond polarization. Here, I would like to draw the attention of the reader to two concepts. The first is the *inductive effect* and the second is the *mesomeric effect*. For a student who knows and understands these two concepts well, it will be easier and more enjoyable to travel along the paths of organic chemistry that seem to be winding.

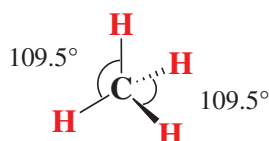
One of the other important points in organic chemistry, after learning bonding theory, is to think of molecules in a three-dimensional environment and estimate their true structures. This is an extremely simple thing. However, in order to understand it, it is necessary to work with simple organic models.

1.2 Covalent Bonding and Hybridization

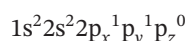
In organic chemistry, unlike in inorganic chemistry, we deal with covalent bonds. Bonds are formed by overlapping of orbitals and the placement of electrons in these orbitals. Let us first look at how a hydrogen molecule is formed. The covalent bond between two hydrogen atoms is formed when the 1s orbital of one hydrogen atom overlaps with the 1s orbital of a second hydrogen atom as shown below. Overlapping orbitals can be pure orbitals as well as hybrid orbitals.



We will begin the discussion with the simplest molecule in organic chemistry, methane (CH_4), with only one carbon atom. It is well known that the carbon atom is located in the center of the methane molecule, and it has four covalent C—H bonds. All the four bonds have the same length, and all bond angles are also the same (109.5°). This structure, which forms a smooth tetrahedron, is called a *tetrahedral* structure.



In the perspective formula, the hydrogen atoms shown with solid lines and the carbon atom are located in the paper plane. The bond represented as a dashed wedge projects behind the plane of the paper. The bond represented as solid wedge projects out of the paper (toward the viewer). To understand this structure of the methane molecule, it is necessary to first examine the electronic configuration of the carbon atom. The electronic configuration of the carbon atom is as follows:



The atomic orbitals of the carbon atom are shown in Figure 1.1. The 2s orbital is drawn larger than the 1s orbital. Because the 2s orbital is in a location more remote from the core, it covers a larger area than the 1s orbital. The energy levels of these orbitals are different. The energy level of the 2s orbital is lower than that of the p orbitals. The energy levels of the 2p orbitals are equal to each other; in other words, they are degenerated.

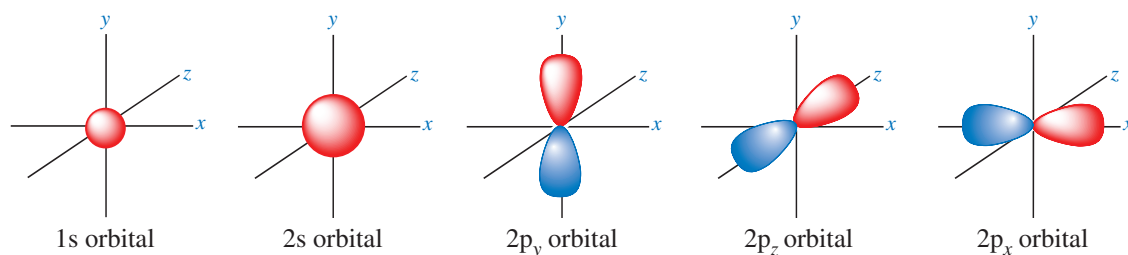


Figure 1.1 Atomic orbitals of the carbon atom.

The carbon atom has only two unpaired electrons in its electronic configuration. This indicates that this atom can form only two covalent bonds, but with two covalent bonds, it would not complete its octet configuration. However, we know that the carbon atom forms four covalent bonds. Now, we need an explanation why carbon forms four covalent bonds. Without unpaired electrons, this configuration does not allow four bonds to be made. With a small amount of energy, one electron from the 2s orbital can be promoted into the empty $2p_z$ orbital (Figure 1.2). This energy is readily compensated for by bond formation.

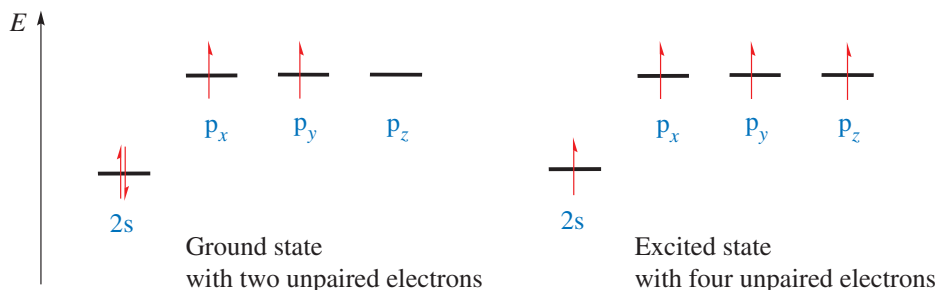


Figure 1.2 Electronic configuration of the carbon atom in the ground state and the excited state.

Now, this configuration of carbon can form four covalent bonds. If carbon uses an s and three p orbitals to form these four bonds, the bond formed with p orbitals will be different from the bond formed with an s orbital. On the other hand,

we know from spectroscopic studies that methane has a tetrahedral structure and the four C—H bonds in methane are identical. We have to answer the question *How can the carbon atom form four identical bonds by using three p orbitals and one s orbital?* Carbon uses the hybrid orbitals. To be able to generate this geometry, the 2s orbital on carbon is mixed with all the three 2p orbitals to make four equivalent sp^3 orbitals with tetrahedral symmetry (Figure 1.3).

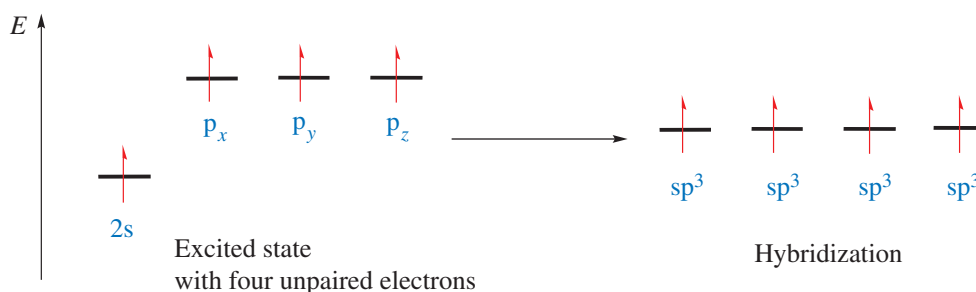


Figure 1.3 Electronic configuration of the carbon atom in the ground state and the hybridized state.

1.2.1 sp^3 -Hybridization of Carbon

Now, we know why the bonds in methane are equal. One s orbital and three p orbitals of the carbon atom combine to form four new orbitals. The concept of combining was proposed by Linus Pauling in 1931. Because the number of combining orbitals is 4, the number of newly formed orbitals is also 4. The phenomenon of orbitals creating new orbitals by combining with each other is called *hybridization*. These new orbitals (hybrid orbitals) are formed by the combination of one s and three p orbitals, and so they are called sp^3 hybrid orbitals. The superscript 3 above the letter “p” indicates that three p orbitals were mixed with one s orbital to form hybrid orbitals. These orbitals are expressed as “s-p-three”; “s-p-cubed” is wrong. The hybridization involved is called sp^3 hybridization. The energies of these hybrid orbitals are equal. The hybrid orbitals formed create a pyramidal structure (tetrahedral) and the angles between the hybrid orbitals are 109.5° (Figure 1.4). The new sp^3 hybrid orbitals consist of two lobes such as the p orbitals. However, the lobes of an sp^3 orbital are not the same size. The larger lobe is used in covalent bond formation. Each sp^3 orbital has a 75% p character and 25% s character. This ratio is very important. As we explain some reactions later in the book, we will return to the s and p ratios of the hybrid orbitals.

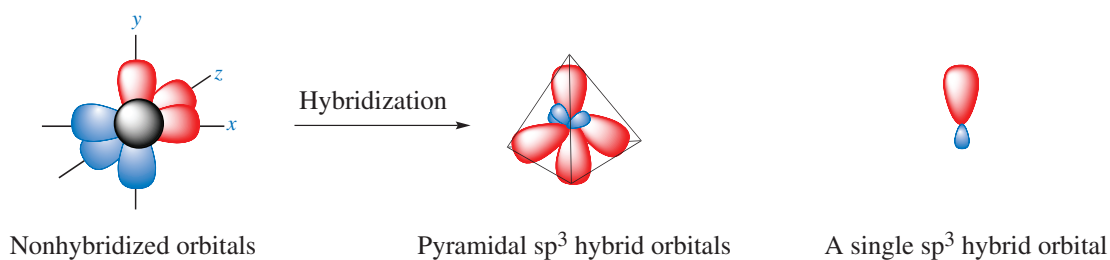
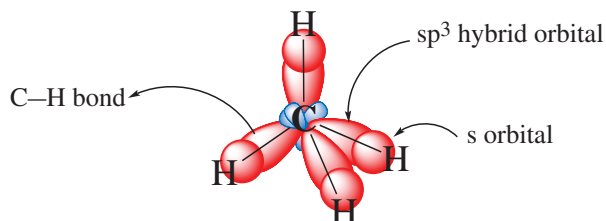
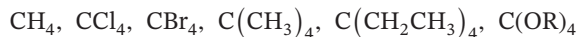


Figure 1.4 Shape of the sp^3 hybrid orbitals.

After explaining hybridization, we can go back to the methane molecule. The bonds between the carbon and hydrogen atoms in the methane molecule are not formed by the combination of pure s or p orbitals. The four sp^3 hybrid orbitals of carbon can combine with four hydrogen s orbitals forming in methane (CH_4). Because the sp^3 hybrid orbitals are equal, the bonds formed by the carbon atom are also equal, and the methane molecule has a pyramidal structure.



If two orbitals overlap along the bond axis (i.e. end-to-end overlap of atomic or molecular orbitals), the bond formed is called a σ bond. In saturated carbon compounds, the bonds that connect atoms are σ bonds, and the hybridization of the carbon atom is always sp^3 . For example, the hybridization of the carbon atom in carbon tetrachloride (CCl_4) is sp^3 . The structure is a pyramidal structure just like in methane, and all carbon–chlorine bonds are equal. In all compounds given below, the angle between the bonds is 109.5° as the substituents are equivalent.



However, if different substituents are attached to the carbon atom, the hybridization of the carbon atom in saturated systems (tetravalent carbon) does not change, but there are some deviations from the ideal tetrahedral structure. The bond angles of some atoms and bond lengths vary according to the connected groups.

After examining the methane molecule, let us apply hybridization to the ethane molecule. In this case, we need to examine each carbon atom separately. Both carbon atoms in ethane are sp^3 hybridized and they are tetrahedral. These hybrid orbitals then combine and form σ -bonds. The ethane molecule has seven σ -bonds. Six of them are σ bonds that bind hydrogen atoms, and they are formed by overlapping of sp^3 hybrid orbitals of carbon atoms with s orbitals of hydrogen atoms. This reveals that σ bonds can also be formed by the combination of different orbitals. The C–C bond is formed by overlapping of one sp^3 orbital of one carbon with an sp^3 orbital of the other carbon (Figure 1.5).

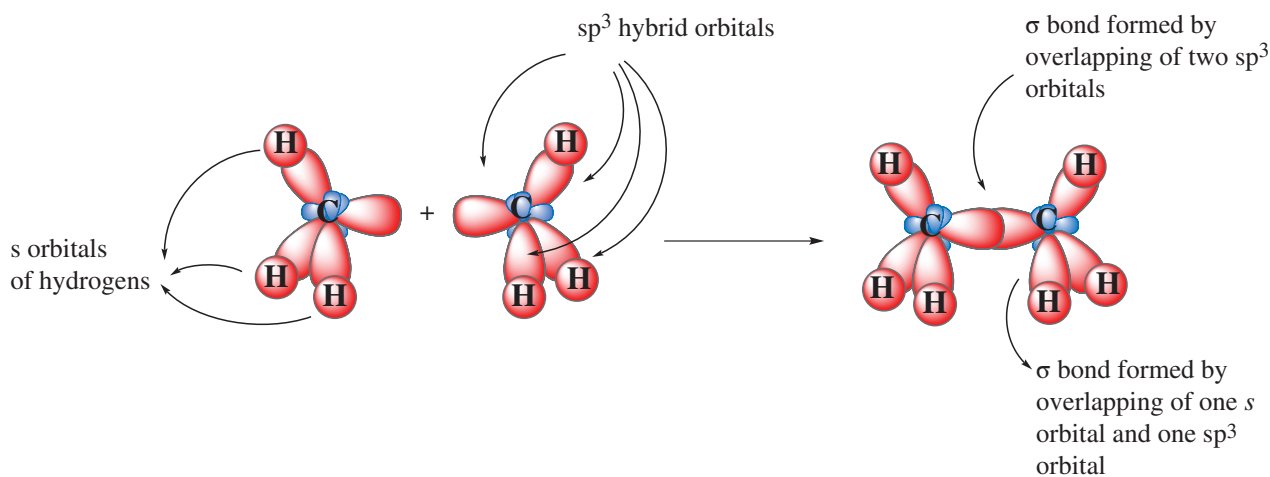


Figure 1.5 Overlap of two sp^3 orbitals to form the carbon–carbon bond in ethane.

What sort of orbitals describe the bonding in compounds such as ammonia and water having bonding and nonbonding pairs of electrons? Let us examine hybridization in ammonia (NH_3). The outer shell of the nitrogen atom consists of one s orbital and three p orbitals, as in the carbon atom. Nitrogen has five valence electrons. According to the basic electronic configuration of the nitrogen atom, the nitrogen has three unpaired electrons, which explains why nitrogen is trivalent, as three covalent bonds are needed for octet formation. Three p orbitals can be used for overlapping with the s orbitals of hydrogen atoms, leaving the nonbonding electrons in the $2s$ orbital. However, this arrangement does not minimize the repulsion between the electrons. The best solution is again sp^3 -hybridization. During the formation of ammonia, one $2s$ orbital and three $2p$ orbitals of nitrogen combine to form four hybrid orbitals having equivalent energy, which is then considered an sp^3 type of hybridization just like the carbon atom (Figure 1.6).

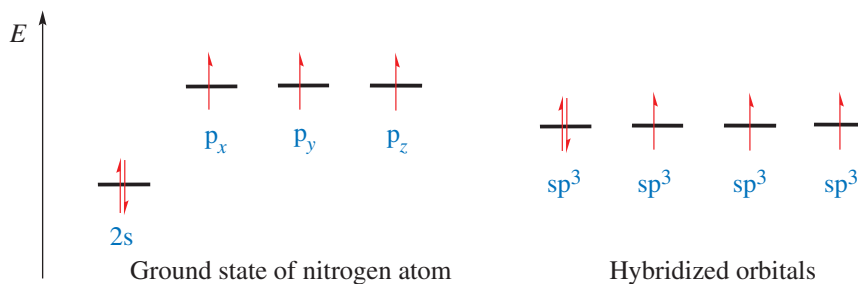


Figure 1.6 The electronic configuration of nitrogen atom in the ground state and the hybridized state.

Three of the sp^3 orbitals are used to bond the hydrogen atoms. The lone electron pair settles in the remaining fourth sp^3 hybrid orbital. This orbital is called a *nonbonding orbital* and the electrons in this orbital are called *nonbonding electrons*. Because the sp^3 hybrid orbitals form a pyramidal structure, the hydrogen atoms attached to the nitrogen atom also form a pyramidal structure. The H—N—H bond angles are 107.3° in ammonia and it has an almost tetrahedral structure. Now, we can understand why ammonia does not have a planar structure (Figure 1.7).

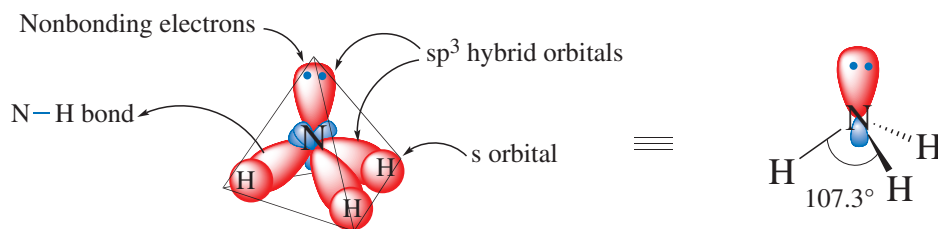
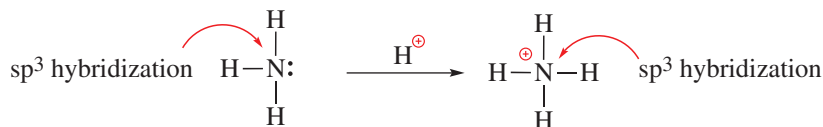


Figure 1.7 Hybridization and bonding in ammonia (NH_3).

The bonds made by nitrogen with hydrogen atoms are equivalent. While three of the four sp^3 hybrid orbitals of the nitrogen atom are used for N—H bonds, the remaining fourth sp^3 orbital contains the lone pair of electrons. Because the four hybrid orbitals in the ammonia molecule are not used equally as they are used in methane, a small deviation from the pyramidal structure occurs. One would expect this angle (107.3°) to be larger than in methane (109.5°) because of the repulsion between hydrogen atoms. As these nonbonding electrons are not shared, they are relatively close to the nitrogen atom. Therefore, they exert increased repulsion on the N—H bond electrons, thereby leading to bond-angle compression. Such a push brings the hydrogen atoms closer together.



When ammonia is treated with an acid (HCl), ammonia will be protonated and an ammonium salt will be formed. Hybridization of the nitrogen atom does not change. It remains as sp^3 . Because four hydrogen atoms are attached to the nitrogen atom, they form a smooth tetrahedron and the angle between the hydrogen atoms changes from 107.3° to 109.5° . When determining hybridization, we need to think of nonbonding electrons like a substituent.

We are faced with a similar situation in the H_2O molecule. It may be thought that this molecule is linear in the first stage. However, we know from the experimental measurements that the bond angle in water is 104.5° . Let us examine the basic electronic configuration of oxygen first. Two of the six electrons in the outer shell are located in the $2s$ orbital. The other four electrons are in the three $2p$ orbitals. Two electrons populate the $2p_x$ orbital. Therefore, oxygen has two unpaired electrons in two $2p_y$ and $2p_z$ orbitals, which reveals why oxygen forms two covalent bonds with other atoms (Figure 1.8).

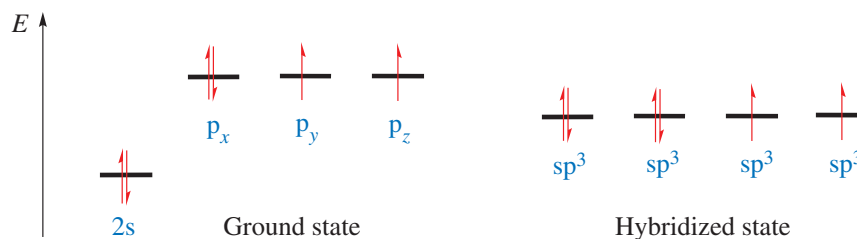


Figure 1.8 The ground-state electronic configuration of the atomic oxygen atom and the hybridized oxygen atom.

Using the atomic orbitals (p orbitals) directly for bonding is not a good model for describing bonding in water, as the angle between the bonds would be expected to be 90° . As mentioned, we know that is not the case. Again, the best solution is sp^3 hybridization. During the formation of water, one $2s$ orbital and three $2p$ orbitals of oxygen combine to form four hybrid orbitals, which is then considered an sp^3 type of hybridization as for the carbon atom. Two sp^3 orbitals are used for

overlapping with the s orbitals of hydrogen atoms, leaving the two pairs of nonbonding electrons in the remaining 2 sp^3 hybrid orbitals (Figure 1.8). Because the sp^3 hybrid orbitals form a pyramidal structure, the hydrogen atoms attached to the oxygen atom with the nonbonding electrons also form a pyramidal structure. The H—O—H bond angle is 104.5° in water and it has an almost tetrahedral structure. Now, we can understand why water does not have a linear structure (Figure 1.9). The H_2O molecule is not linear but angular. The repulsions between lone pairs and bonding pairs is expected to be greater, causing the H—O—H bond angle to be smaller than the ideal 109.5° .

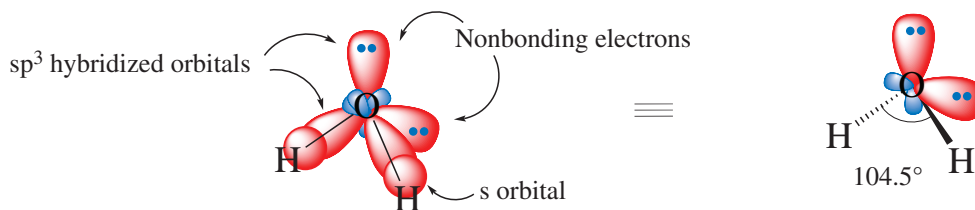


Figure 1.9 Hybridization and bonding in the H_2O molecule.

1.2.2 sp^2 -Hybridization of Carbon

Before examining sp^2 -hybridization, let us briefly consider the overlap of the orbitals and how double bonds are formed. Orbitals can overlap in two ways:

1. Head-to-head overlap
2. Side-to-side overlap

So far, we have seen the head-to-head overlap of different orbitals. Head-to-head overlap of atomic orbitals or hybridized orbitals generates σ bonds where the electron density is centered along the internuclear axis. As one can see from Figure 1.10, pure orbitals as well as hybridized orbitals can interfere and form σ bonds. The electrons in these orbitals are called σ electrons.

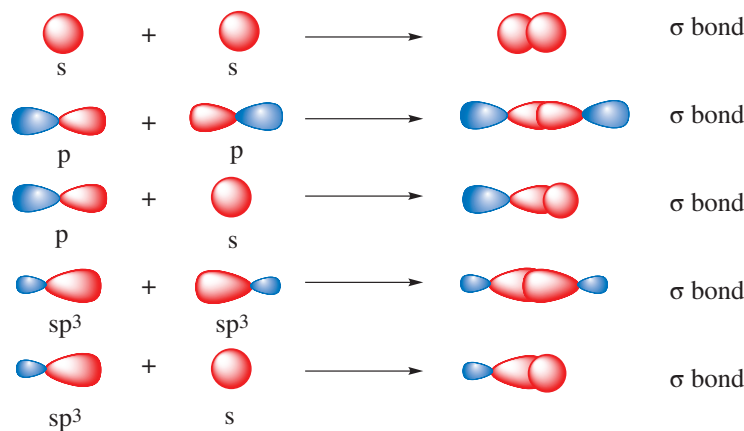


Figure 1.10 Formation of σ bonds by head-to-head overlap of different orbitals.

We have discussed the formation of a σ bond between different elements. The question is: *Is it possible to make a double bond between the carbon atoms and how can we do it?* The two carbon atoms are most easily connected along the axis via σ bonds. Because a σ bond fills the space between the two carbon atoms with electrons, it is not possible to connect these atoms with a second σ bond by head-to-head overlap. Therefore, the two carbon–carbon bonds in a double bond cannot be identical and so the second or third bonds must be different from the σ bond. The second bond of the double bond in ethylene can be constructed from side-to-side overlap of pure p orbitals of each carbon atom. Some elements use their d orbitals to form a bond.

Since there is no d orbital in the carbon atom, we will not examine the overlap with d orbitals here. However, these overlaps are important in inorganic elements having d orbitals such as sulfur and phosphorus. As can be seen in Figure 1.11,

p orbitals can overlap side-to-side to form a new bond above and below the axis that connects atoms. This bond is called a π bond. π Bonds are formed by the overlap of pure p orbitals (unhybridized orbitals). The electrons that make up π bonds are called π electrons.

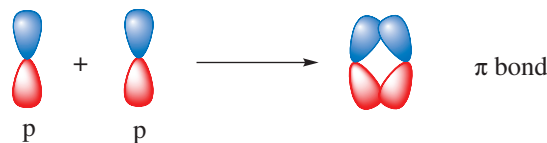
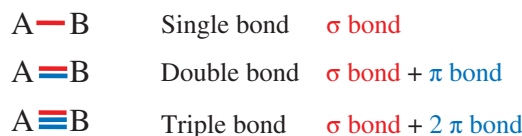
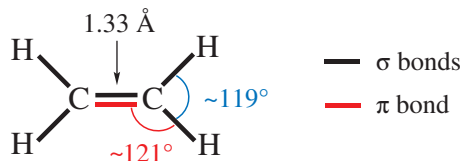


Figure 1.11 The formation of the second C–C bond by side-to-side overlap of pure p orbitals.

Now, let us try to form a double bond between the two carbon atoms. In organic chemistry, two elements can be connected by single, double, or triple bonds. For these bonds, two, four, and six electrons are needed, respectively. Regardless of the number of bonds, one of these bonds is definitely a σ bond. Because σ bonds are axially connecting the atoms, there cannot be more than one bond on this line. The second and third bonds are formed only through pure p orbitals, and these bonds are π bonds. Thus, we can make the following generalization:



If there is a single bond between the two atoms, this bond is always a σ bond. When there are two bonds, one is a σ bond and the other is a π bond. In triple bonds, the first bond is a σ bond and the other two are π bonds. This rule always holds. Before we create a double bond between two carbon atoms, let us first examine the ethylene molecule, the smallest member of carbon compounds containing a double bond. The angle between the hydrogen atoms is approximately 119° and the angle between the H–C=C atoms is 121° .



Each carbon is bonded to three atoms. As one of the pure p orbitals will be used for the π bond, the remaining orbitals, an s orbital and two of the p orbitals, will hybridize (Figure 1.12).

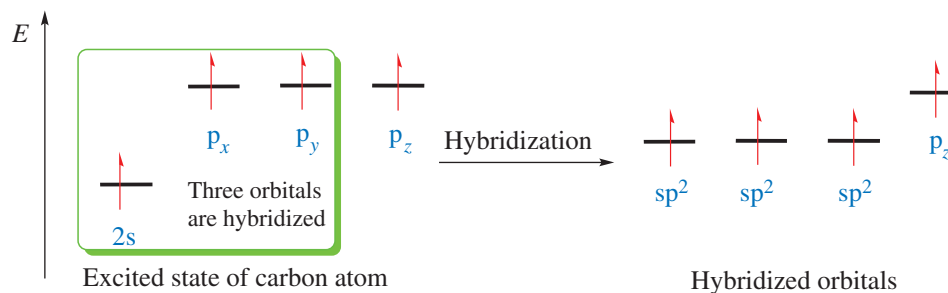


Figure 1.12 sp^2 -Hybridization.

Let us examine the orbitals in the second shell of the carbon atom again. They are an s orbital and three p orbitals oriented in the x, y, and z directions. Now, we remove any of these p orbitals, which will be used for making the double bond, and examine the position of the remaining orbitals. The remaining orbitals (1 s and 2 p orbitals) are located in a plane (Figure 1.13). The s orbital is also in this plane because of its spherical structure. In the ethylene molecule, carbon atoms make three σ bonds apart from the π bond. If carbon uses an s and two p orbitals to form the bonds with carbon and hydrogen atoms, the bond formed with p orbitals will be different from the bond formed with the s orbital. We would expect

to have an angle of at least 90° between the two groups bound to the carbon atom via p orbitals. However, it is known that the angles between the groups bound to carbon in the ethylene molecule are approximately 120° . This observation reveals that the carbon atom does not use pure orbitals when forming the σ bonds.

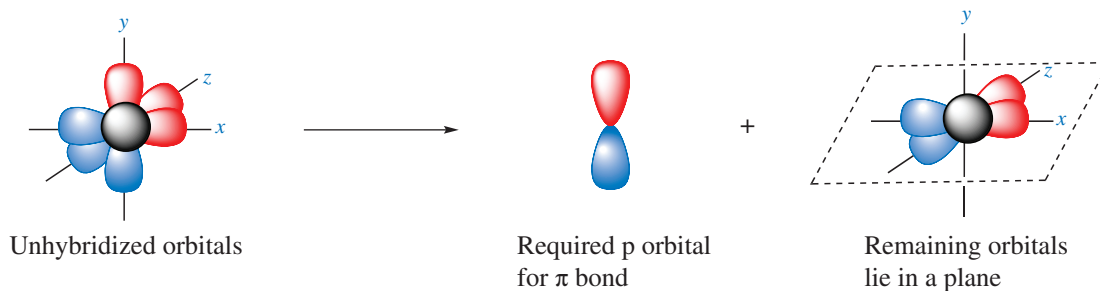


Figure 1.13 Unhybridized carbon orbitals.

This can only be explained in the ethylene molecule by hybridization. Now, these three orbitals, a single 2s orbital and two 2p orbitals, undergo hybridization and three new hybrid orbitals are formed. These orbitals are called sp^2 hybrid orbitals. These orbitals have the same shape and the electrons in each orbital have the same energy and they lie in a plane. To minimize electron repulsion, the three sp^2 orbitals need to get as far from each other as possible. These hybrid orbitals are separated by 120° and they are directed toward the corners of a triangle (Figure 1.14). This type of hybridized orbital is called an sp^2 (pronounced “s-p-two” not “s-p-squared”) orbital.

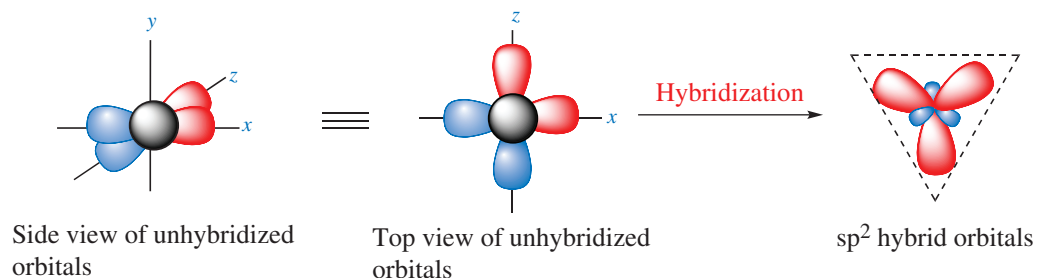


Figure 1.14 Orbitals before and after sp^2 hybridization.

The carbon atoms in ethylene form two bonds with each other. Two bonds connecting two carbon atoms are called a *double bond*. Let us try to explain how this double bond is formed. One of them, a σ bond, results from the overlap of an sp^2 -hybrid orbital of one carbon with an sp^2 -hybrid orbital of the other carbon ($sp^2 + sp^2$). This bond is formed by head-to-head overlap. The second C—C bond, a π bond, results from side-to-side overlap of the two unhybridized p orbitals, which are perpendicular to the plane formed by sp^2 hybrid orbitals. These two p orbitals must align parallel to each other so that a maximum overlap can occur. Each carbon uses the remaining sp^2 orbitals to overlap with an s orbital of a hydrogen to form the C—H bonds (Figure 1.15). As the π bond is perpendicular to the plane, π electrons are located above and below this plane.

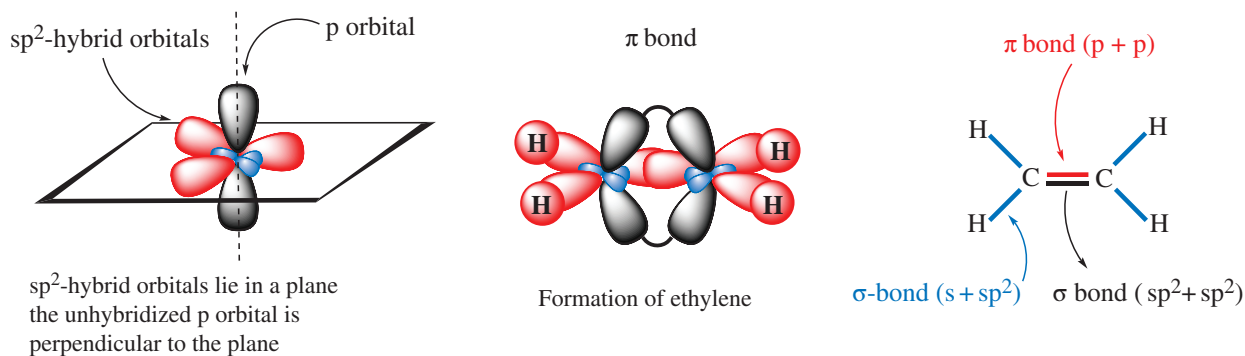


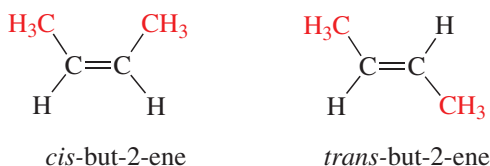
Figure 1.15 Formation of an ethylene molecule.

Because the three new sp^2 orbitals formed are equal, the bond angles should be 120° . However, because two different atoms (one carbon, two hydrogens) are connected to the double-bond carbon atom in ethylene, the σ bonds are not equal and a slight deviation from the ideal geometry is observed.

After discussion of sp^2 -hybridization, we can make a generalization. Atoms bonded to a double-bond carbon with a σ bond (whatever atom) including the double-bond carbon atoms are located in the same plane.

In ethylene, the carbon atoms are held by four electrons. However, in the case of a C—C single bond, only two electrons hold the carbons together. Therefore, a C=C double bond is stronger (174 kcal/mol or 728 kJ/mol) and shorter (1.33 Å) than a C—C single bond (90 kcal/mol or 377 kJ/mol, and 1.54 Å).

Rotation around a single bond occurs readily at room temperature, while rotation around a double bond is restricted. Restricted rotation of groups attached to the double bond causes a new type of isomerism as shown below. *cis*- and *trans*-But-2-ene are isomeric compounds, and they have different physical and chemical properties.



Just like π bonds formed between carbon–carbon atoms, π bonds can also be formed between carbon and heteroatoms. For example, let us consider a double bond in a carbonyl group. We are going to look at the bonding in acetone, but it could equally apply to any other compound containing C=O. The interesting thing is the nature of the carbon–oxygen double bond, not what it is attached to. The hybridization of the carbon atom will be of course sp^2 . Oxygen will form a double bond with the carbon atom, which indicates that the oxygen atom will use one of the p orbitals for making the double bond. The remaining one s and two p orbitals undergo sp^2 -hybridization as well. While one of the sp^2 -hybrid orbitals forms the σ bond with the sp^2 hybrid orbital of the carbon atom, the four nonbonding electrons settle in the empty sp^2 hybrid orbitals (Figure 1.16).

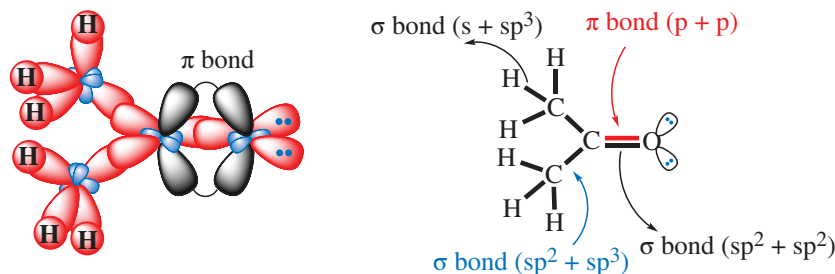


Figure 1.16 Hybrid orbitals of acetone.

The distribution of electrons in the π bond is heavily distorted toward the oxygen end of the bond because oxygen is much more electronegative than carbon. Because the hybridization of the carbon and oxygen atom in acetone is sp^2 , all the carbon atoms lie in a plane. For example, starting from the structure of acetone, it should not be difficult to guess that formaldehyde ($\text{CH}_2=\text{O}$) has a planar structure.

1.2.3 sp -Hybridization of Carbon

As we mentioned above, some molecules have triple bonds between two atoms. For example, nitrogen atoms in the nitrogen molecule are connected by a triple bond. In organic chemistry, carbon atoms can also be connected to each other via a triple bond. As the simplest example, we can give the acetylene molecule. A triple bond can also be formed between carbon and nitrogen atoms (as in nitrile compounds).



How is a triple bond formed? As we have discussed above, the two atoms can form only one σ bond along the axis that connects them. Furthermore, we explained that the second bond is a π bond. Therefore, the third bond must also be a π

bond. In acetylene, carbon atoms form a triple bond using two pure p orbitals. The remaining s and p orbitals are hybridized to form two sp hybrid orbitals (Figure 1.17).

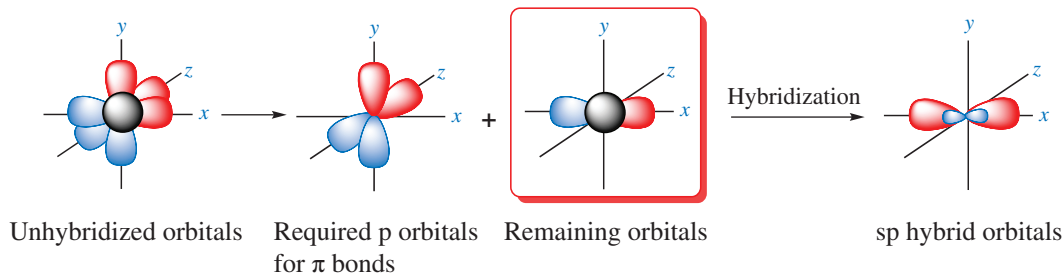


Figure 1.17 sp Hybrid orbitals.

The remaining p orbitals are not hybridized. The sp orbitals have the same shape but they point in the opposite direction, and the bond angles between them are 180° again to provide maximum separation of electrons. The two p orbitals that are not hybridized are perpendicular to the axis that passes through the center of the carbon atoms. They will form the two π bonds. The two p orbitals on each carbon atom overlap side-to-side to form the π bonds. One of the sp orbitals of one carbon in acetylene overlaps with an sp orbital of the other carbon to form a C—C σ bond. The remaining sp orbital overlaps with the s orbital of the hydrogen atom to form a C—H σ bond (Figure 1.18). Because the angle between the sp hybrid orbitals is 180° , the acetylene molecule has a linear structure.

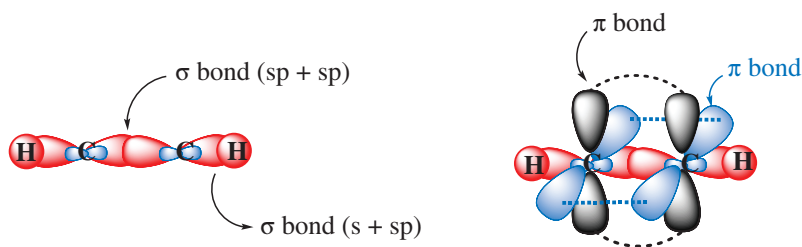


Figure 1.18 Hybrid orbitals of acetylene.

Nitrogenous compounds can also form triple bonds. The nitrogen molecule (N_2) is an "unusually stable" compound, particularly because nitrogen forms a triple bond with itself. The nitrogen atom has five valence electrons, and so it needs three more electrons to complete its octet. It is possible either to bond three atoms forming three covalent bonds or to share three electrons with another nitrogen atom, forming a triple bond. In fact, the triple bond in nitrogen is one of the strongest bonds known. Of course, nitrogen can also form a triple bond with the carbon atom. For example, acetonitrile ($CH_3-C\equiv N$) has a triple bond between nitrogen and carbon atoms. The hybridization of both nitrogen and carbon atoms is sp. The nonbonding electrons of nitrogen are in the sp hybrid orbital. The σ bond between the two carbons is formed by overlap of an sp orbital and sp^3 hybrid orbitals, and the two carbon atoms and nitrogen atom are located on a line.

In order for hybridization to be sp in a carbon atom, it is not necessary for the carbon atom to form a triple bond. For example, let us examine a compound of the cumulene type, compounds with two double bonds attached to a carbon atom such as allenes, isocyanates, and ketenes.



Allene



Isocyanate



Ketene

The cumulated double bonds give allenes an unusual geometry because of the sp hybridization of the central carbon atom. In allenes, the two terminal carbons are sp^2 -hybridized. One of the unhybridized p orbitals of the central carbon atom overlaps with a p orbital of an adjacent sp^2 carbon atom. The second p orbital of the central carbon atom overlaps with a p orbital of the other sp^2 -hybridized carbon atom so that the central carbon atom produces two π bonds. These π bonds are perpendicular and so the molecule is twisted (Figure 1.19). An interesting consequence of this configuration is that allenes having two different substituents on each of the terminal carbon atoms are chiral.

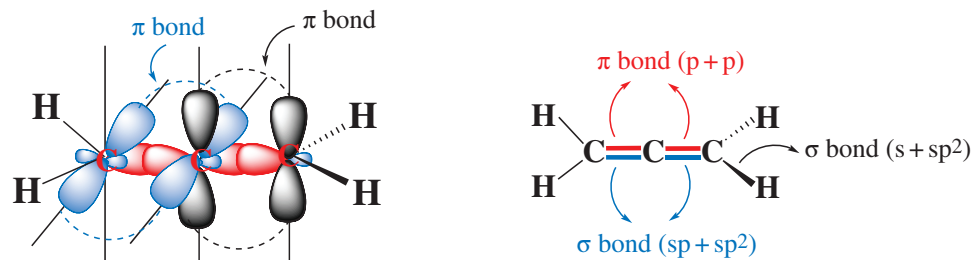


Figure 1.19 The structure of allenes and hybridization of the bonds.

Cumulenes may also have more than two double bonds. For example, 1,2,3-butatriene ($\text{CH}_2=\text{C}=\text{C}=\text{CH}_2$) and 1,2,3,4-pentatetraene ($\text{CH}_2=\text{C}=\text{C}=\text{C}=\text{CH}_2$) also belong to the cumulene class. The carbon atoms in such compounds all have a linear structure. However, the configuration of the terminal substituents depends on the number of double bonds. For an even number of double bonds, as in allene, an orthogonal configuration of terminal substituents will be seen. For an odd number of double bonds, the terminal substituents and all the carbons will lie in a plane.

After examining the hybridization of neutral compounds, let us briefly discuss the hybridization of ionic compounds (carbocations and carbanions) and radicals. Carbocations are carbon compounds that carry a positive charge on a carbon atom, which is attached to three groups. For example, positively charged carbon in the methyl cation is bonded to three hydrogen atoms and the hybridization of the carbon atom is sp^2 . Therefore, the carbon atom forms three covalent bonds by using the three sp^2 hybrid orbitals. The remaining p orbital is empty and perpendicular to the plane formed by hydrogen and carbon atoms (Figure 1.20).

Radicals are molecules that contain at least one unpaired electron. The hybridization of the carbon atom in the methyl radical is also sp^2 . The methyl radical differs from the methyl cation by having one unpaired electron, which is located in the p orbital. The p orbital is perpendicular to the plane formed by methyl protons and the carbon atom.

The situation is different in carbanions. The structure of the methyl anion can be compared with the electronic structure of ammonia. The hybridization of the carbon atom is sp^3 . Three of the sp^3 hybrid orbitals overlap with the s orbital of hydrogen, forming σ -bonds. The remaining sp^3 orbital holds the electrons (Figure 1.20).

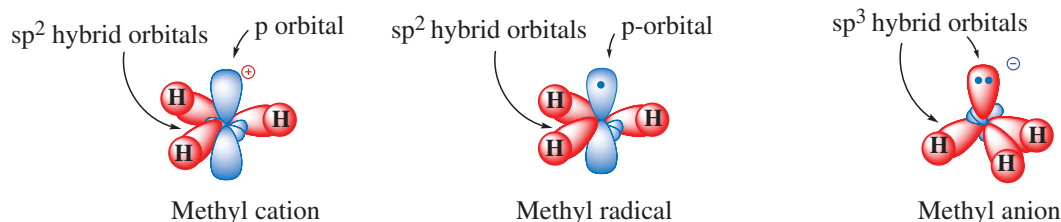


Figure 1.20 Hybridization in methyl cation, methyl radical, and methyl carbanion.

We can summarize what we have seen so far as follows. Single bonds are always made from σ bonds. One of all double bonds is a σ bond, and the other is a π bond. Triple bonds consist of two π bonds and one σ bond. The simplest method to determine the hybridization of a carbon atom or any heteroatom is to look at the number of π bonds that the atom has formed. If the atom does not form any π bonds, the hybridization is sp^3 , and if there is one π bond, then the hybridization is sp^2 . In the case of having two π bonds, the hybridization is sp .

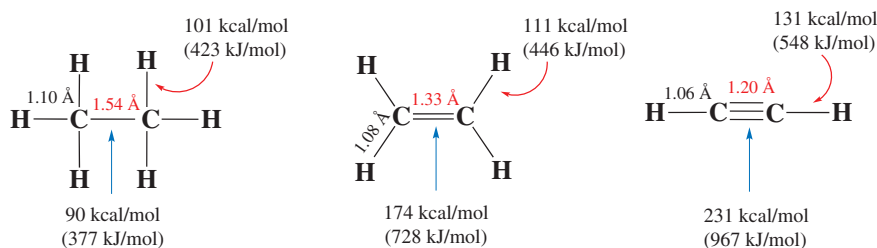
1.2.4 Bond Lengths

After examining bond structures, let us take a brief look at bond lengths and bond energies. Bond energies are directly related to the reactivity of molecules. As the number of bonds connecting the two atoms increases, the distance between the atoms becomes shorter. Triple bonds are shorter than double bonds and double bonds are shorter than single bonds. The hybridization affects the C—C and C—H bond lengths (Table 1.1).

Table 1.1 The bond distances between carbon and heteroatoms in Å.

	C	N	O	Type of bonding
C	1.54	1.47	1.43	Single bond
	1.33	1.28	1.23	Double bond
	1.20	1.21	—	Triple bond
N	1.47	1.46	1.41	Single bond
	1.28	1.25	1.14	Double bond
	1.16	1.10	—	Triple bond
O	1.43	1.41	1.49	Single bond
	1.23	1.14	1.21	Double bond

The carbon–carbon single bond is 1.54 Å in length, the double bond is 1.33 Å, and the triple bond is around 1.20 Å. Interestingly, C–H bonds are generally much shorter and stronger than C–C single bonds. This is because the s orbital of hydrogen is closer to the nucleus than is the sp^3 orbital of carbon. The length and strength of a C–H bond depend on the hybridization of the carbon atom to which the hydrogens are connected. The more s characteristic used in the orbital of carbon to make a bond, the shorter and stronger the bond is. Therefore, a C–H bond in ethane formed by overlap of a sp^3 -hybridized orbital (25% s ratio) is longer and weaker than a C–H bond formed by overlap of an sp^2 hybridized orbital (33.3% s ratio). On the other hand, a C–H bond formed by overlap of an sp hybrid orbital is shorter and stronger than the other bonds. For example, the C–H bond in acetylene (1.06 Å) is shorter than the C–H bond in ethylene (1.08 Å). The C–H bond in ethane (1.10 Å) is longer. Generally, s orbitals are spherical (more compact) and closer to the atomic nucleus. When the distance between two atoms is short, the electron density is high and the bond is stronger.



Let us compare the energies of carbon–carbon single bonds with those of carbon–carbon double bonds. A C=C double bond (174 kcal/mol) in ethylene is stronger than a C–C bond (90 kcal/mol) in ethane. As one can see, the C=C double bond of ethylene is not twice as strong. Let us calculate how strong the π bond is compared to a σ bond. The strength of the σ bond in ethane formed by sp^3 – sp^3 overlap is 90 kcal/mol. The strength of the σ bond in ethylene cannot have this value because that bond is formed by sp^2 – sp^2 overlap. Therefore, it must be stronger because of the increased s ratio in the overlapping orbitals. Experiments reveal that the energy of the σ bond in ethylene is approximately 112 kcal/mol. Now, we can calculate the strength of the π bond as $174 - 112 = 62$ kcal/mol. As expected, the π bond is weaker than the σ bond because of the side-to-side overlap. As a consequence of this bond weakness, π bonds undergo chemical reactions more easily than σ bonds do.

1.3 Electrophiles and Nucleophiles

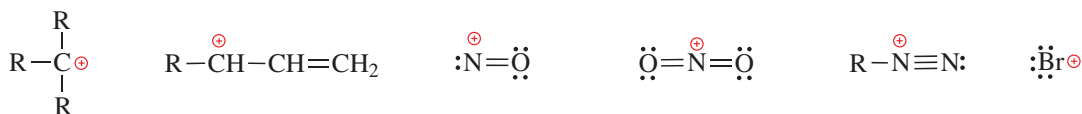
There are some basic concepts in organic chemistry that need to be learned before moving on to the reaction mechanisms. Once the basic concepts have been firmly grasped, the reaction mechanisms will be better understood. Therefore, in this section, we will primarily focus on these basic concepts.

1.3.1 Electrophiles (Electrophilic Compounds)

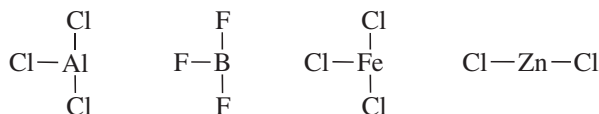
Chemical reactions are those that are based on electron exchange. During a chemical reaction, one compound donates electrons and the other accepts them. For a compound to accept electrons, it must be electron deficient. Therefore, to understand how the functional groups react, we must first learn to determine electron-deficient and electron-rich atoms and molecules. Electron-deficient atoms and molecules, which can take electrons, are called electrophilic compounds or *electrophiles*. Electrophile literally indicates electron loving. Electrophiles react with electron-rich compounds and try to achieve a stable shell of electrons like that of a noble gas. We can categorize electrophilic compounds in various groups.

- Cations (compounds that contain a positive charge)
- Lewis acids
- Carbonyl compounds
- Compounds containing polarized bonds

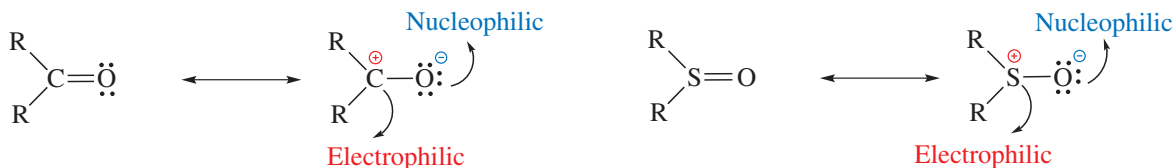
Cations: All atoms or molecules such as carbon, nitrogen, and halogens that have lost one or more valence electrons form an ion with a positive charge. For example, all carbocations (a more detailed description of carbocations is given in the carbocation section) with sp^2 -hybridization and bound to three substituents are electrophiles. They are electron-deficient compounds. By reacting with nucleophiles, they accept electrons to neutralize the positive (+) charge and form a stable electronic configuration. Some examples of electrophiles having a positive charge are given below.



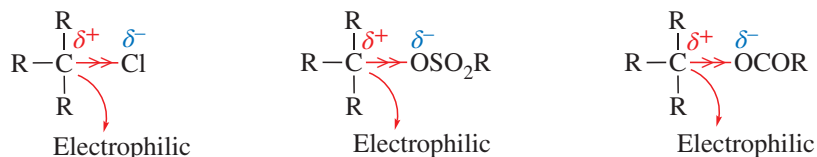
Lewis acids cannot deliver protons like classical acids. Compounds that are electron deficient are included in this group. Molecules with an incomplete octet of electrons such as AlCl_3 , BF_3 , and FeCl_3 can act as a Lewis acid. Generally, the number of electrons in the outer shell of these compounds is six. These compounds can easily react with electron-rich compounds and accept an electron pair to fill its valence shell.



Carbonyl compounds are also potential electrophilic compounds. Double-bond electrons between carbon and oxygen are polarized because of the fact that oxygen is more electronegative than carbon. There is a partial positive charge on the carbon and a partial negative charge on the oxygen. The resonance structure of a carbonyl group is shown below to emphasize the charge separation in the carbonyl group. The structure has only one bond between the carbon and oxygen. In this structure, oxygen has an octet but carbon does not. Consequently, carbonyl carbon shows electrophilic properties and reacts easily with nucleophiles. The double bond between sulfur and oxygen is also polarized and sulfur shows electrophilic properties.



Apart from these compounds, any compound with bond polarization shows electrophilic properties. For example, alkyl halides contain a polarized σ bond between carbon and halogen atoms because halogens are more electronegative than carbon atoms. The halogens attract carbon-halogen bond electrons toward themselves. Consequently, the carbon atoms are partially positively ($\delta+$) charged, while the halogens are negatively ($\delta-$) charged. For this reason, the carbons bound to the halogen atom have electrophilic properties and react easily with nucleophiles. Strong electron-withdrawing groups such as tosyl and acetoxy groups also make the carbon atom to which they are attached electrophilic as they also attract the bonding electrons toward themselves.

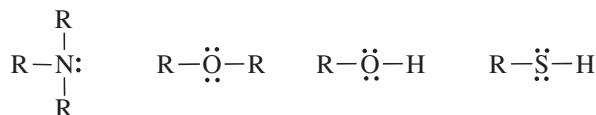


1.3.2 Nucleophiles (Nucleophilic Compounds)

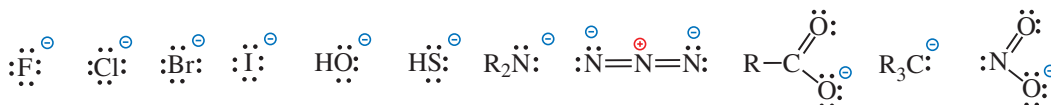
Nucleophiles are chemical species that donate electrons to form a chemical bond and they attack electron-deficient regions in chemical reactions. Nucleophiles are “nucleus loving” compounds. We can classify nucleophiles in different groups.

- Compounds having lone pairs
- Olefinic and aromatic compounds
- Anions and Lewis bases

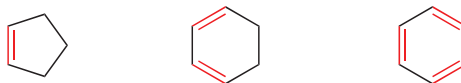
All elements in the fifth and sixth groups of the periodic table contain nonbonding electrons. All of these fall into the nucleophilic compound class because there are electrons in their outer shell and they react easily with electrophiles. For example, compounds such as amines, ethers, alcohols, and mercaptans are the most important representatives of this group. These compounds belong to the Lewis base group as well.



Anions also fall into the nucleophile group because they are negatively ($-$) charged and react easily with electrophiles.



Carbon-carbon double bonds are compounds in which the electron density is rich. They donate a pair of electrons as well. This not only covers double bonds but also triple bonds (alkynes) and even enols and enolates. Aromatic compounds are electron-rich compounds because they have π electrons that are freely delocalized. As these compounds react easily with electrophiles, they are also considered nucleophiles.



1.4 Inductive and Mesomeric Effects

1.4.1 Inductive Effect

In the introductory section, we emphasized that the inductive and mesomeric effects should be learned very well in order to understand the reaction mechanisms and the estimation of possible reaction products, etc., because these are the factors that directly determine and affect the electron density in various regions of the molecule. In symmetrical σ bonds (bonds formed between the same atoms), the electron density is equally distributed between the two atoms because they have the same tendency to attract the bonding electrons. For example, in compounds such as hydrogen, chlorine, bromine, and ethane, the bond electrons are not polarized; they are homogeneously distributed between the two atoms.




If atoms are different from each other, bond electrons are attracted more strongly by one of the atoms and the distribution of the electron density varies. Let us consider a σ bond that binds A and B atoms. If atom A is more electronegative than


atom B, A will attract electrons toward itself and will decrease the electron density around atom B, while the electron density around A will increase. A polar bond is a covalent bond in which there is a separation of charge between one end and the other. One end of the bond is slightly positively polarized and the other slightly negatively polarized. Partial charges are indicated by “ δ ” (delta). The signs δ^+ and δ^- indicate partial charges.



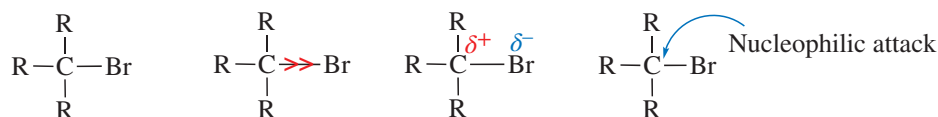
While atom B becomes electrophilic because of bond polarization, atom A is nucleophilic. The presence of the partial negative and positive charges on these atomic centers makes them liable to be attacked by other charged groups or atoms. This bond polarization determines where electrophiles and nucleophiles attack. To determine how a bond between the two atoms is polarized, it is sufficient to look at a table showing electronegativities. With simple rules, it is easy to estimate which element is more electronegative relative to the location of the elements in the periodic table. The electronegativities of some elements that are important in organic chemistry are given in Table 1.2. As is known from general chemistry classes, electronegativity increases from left to right within a row and decreases in a group from top to bottom in the periodic table.

Table 1.2 Electronegativities of selected elements.

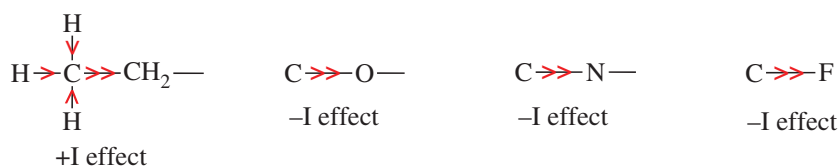
H 2.1							 Increasing electronegativity
Li 1.0	Be 1.6	B 2.0	C 2.5	N 3.0	O 3.4	F 4.0	
Na 0.9	Mg 1.3	Al 1.6	Si 1.9	P 2.2	S 2.6	Cl 3.2	
K 0.8	Ca 1.0				Se 2.4	Br 3.0	
Rb 0.8	Sr 1.0					I 2.7	


 Increasing electronegativity

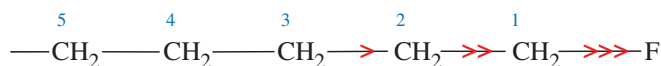
One of the best examples we can give for bond polarization is alkyl halogen bonds. As can be seen from Table 1.2, halogens (F, Cl, Br, and I) are more electronegative than the carbon atom; they attract bonding electrons and polarize the C-halogen bonds. The carbon atom is then partially positively charged and halogens are negatively charged. This charge distribution (polarization) is responsible for all kinds of chemistry of alkyl halides.



If an element is more electronegative than hydrogen, this indicates that it attracts more electrons than hydrogen does, the inductive effect of that element is (–), and the effect is shown as –I. If the element is less electronegative than hydrogen, that is, it repels electrons, the inductive effect of the element is (+) and is indicated as +I. In general, the inductive effects of various substituents are (–) because the electronegativity of almost all the elements bound to the carbon atom is higher than that of hydrogen. However, the inductive effects of the alkyl groups are (+). The electron donor feature of the alkyl groups can be explained as follows. Hydrogen atoms attached to the methyl carbon atom are electron donors relative to the carbon atom. Therefore, the hydrogen–carbon bond polarizes toward the carbon atom and the electron density increases around the carbon atom. When the electron density on carbon increases, this carbon atom repels electrons toward the neighboring carbon atom to reduce the electron density.

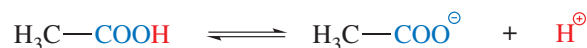


The inductive effect is transmitted only through σ electrons. Let us try to explain the inductive effect in more detail with a fluorine atom attached to the end of a saturated carbon chain. Because the fluorine atom is more electronegative than the carbon atom, it is partially negatively (δ^-) charged by attracting electrons toward itself. The carbon atom C1, whose electrons are drawn, is partially positively (δ^+) charged. We describe this situation as bond polarization.



The partially positively (δ^+) charged carbon atom C1 withdraws bond electrons from the neighboring carbon atom, C2, to remove the reduced electron density around itself. However, this withdrawal is never at a level to neutralize the (+) charge on the carbon atom C1. When C1 pulls bond electrons from C2, C-2 will also be partially positively (δ^+) charged, and the C1—C2 bond will also be polarized. However, the positive (δ^+) charge formed on C2 is never as much as that on C1. C-2 behaves similarly, drawing electrons from C3. C3 is also partially positively (δ^+) charged. *For how many atoms does this last?* The inductive effect usually loses its effect after the third bond. The effect is not observed after the fourth and fifth bonds. The inductive effect propagates through the σ skeleton and drops exponentially from one carbon to another.

It is possible to show through some experiments that the inductive effect decreases exponentially on a chain. As we will discuss in the acid–base part in detail, the substituents significantly affect the $\text{p}K_{\text{a}}$ values of organic acids. An organic acid turns into a carboxylate ion by removing the proton, as shown below. The farther this balance shifts to the right, the greater the acid strength is. The greater acidity of acetic acid is the result of resonance stabilization of the acetate anion.



There is a negative charge ($-$) on the carboxylate ion. If this charge can be distributed over groups bound to the acid functional group, the anion can be stabilized. In general, there are two ways to stabilize the positive (+) or negative ($-$) charges: either neutralize these charges or distribute them as much as possible over other groups. In order to distribute the negative ($-$) charge over other groups, the groups must have electron-withdrawing substituents.

For example, the $\text{p}K_{\text{a}}$ value of acetic acid is 4.86. When one of the methyl protons in acetic acid is replaced by a halogen, the carboxylate anion formed will be stabilized because of the inductive effect of halogen. The strength of the acid will increase, and the corresponding $\text{p}K_{\text{a}}$ value of the acid will decrease. The change in $\text{p}K_{\text{a}}$ values is directly proportional to the inductive effect of halogen. It can be seen from Table 1.3 that the strongest acid is fluoroacetic acid because fluorine is the most electronegative element. In the second group of acids, the $\text{p}K_{\text{a}}$ value of butanoic acid is compared with the $\text{p}K_{\text{a}}$ values of chlorobutanoic acids. If the chlorine atom is bound to the carbon atom C2, the $\text{p}K_{\text{a}}$ value drops from 4.86 to 2.80. This is a very important change. It shows that the inductive effect of chlorine is very important; it can stabilize the anion. When the chlorine atom is attached to the carbon atom C3, a significant change in the $\text{p}K_{\text{a}}$ value is observed. This time, the $\text{p}K_{\text{a}}$ value rises from 2.86 to 4.06, which indicates that the strength of the acid decreases. This value shows that the inductive effect of the chlorine atom decreases significantly as the carbon chain is extended. The change in $\text{p}K_{\text{a}}$ value is quite small when the chlorine atom is bound to the carbon atom C4. If we extend the carbon chain by one more carbon and connect the chlorine atom to the carbon atom C5, this time we will see that the chlorine atom has no effect on the $\text{p}K_{\text{a}}$ value. Finally, observe that the effect falls off quite quickly as the attached halogen gets further away from the $-\text{COO}-$ end. This table clearly shows that the inductive effect is transmitted through the σ bonds and the effect drops exponentially within the three bonds.

Table 1.3 $\text{p}K_{\text{a}}$ values of some carboxylic acids.

Acid	$\text{p}K_{\text{a}}$	Acid	$\text{p}K_{\text{a}}$
CH_3COOH	4.86	$\text{CH}_3\text{CH}_2\text{CH}_2\text{COOH}$	4.82
FCH_2COOH	2.59	$\text{CH}_2\text{CH}_2\text{CH}(\text{Cl})\text{COOH}$	2.84
ClCH_2COOH	2.87	$\text{CH}_3\text{CH}(\text{Cl})\text{CH}_2\text{COOH}$	4.06
BrCH_2COOH	2.90	$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}(\text{Cl})\text{COOH}$	4.56
ICH_2COOH	3.18		

Another important example that experimentally shows how the inductive effect changes along the σ skeleton is the chemical shift values observed in the $^1\text{H-NMR}$ spectra of the compounds. The $^1\text{H-NMR}$ chemical shifts of compounds reflect a linear correlation between the electron density and the chemical shifts. For example, the terminal methyl protons of an alkyl chain resonate at 0.9 ppm. When the carbon atom C2 is replaced by an oxygen atom, the oxygen atom inductively attracts electrons and the electron density around the methyl group decreases. Thus, the resonance signal of the terminal methyl protons shifts from 0.9 to 3.3 ppm. The change observed in the chemical shift is 2.4 ppm. This value is a significant change in NMR spectroscopy. When the carbon atom C3 is replaced with an oxygen atom, the chemical shift of the terminal methyl group appears at 1.3 ppm. The chemical shift's change is now 0.4 ppm. This clearly indicates that the inductive effect of the oxygen atom on the methyl protons decreases significantly in the C3 position. In the C4 position, the effect drops to 0.1 ppm and then to zero. This example again shows that the inductive effect changes exponentially from one carbon to another.

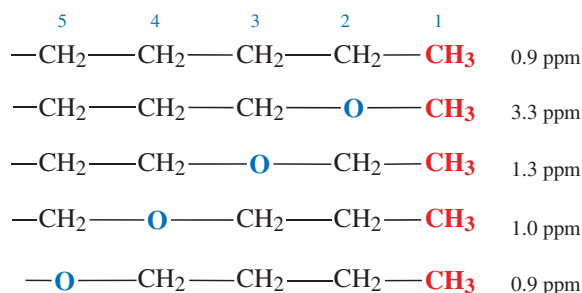


Table 1.4 The types of inductive effect: functional groups.

-I Groups			+I Groups	
$-\text{NH}_3^+$	$-\text{CHO}$	$-\text{SH}$	$-\text{CH}_3$	$-\text{COO}^-$
$-\text{NR}_3^+$	$-\text{COR}$	$-\text{SR}$	$-\text{CH}_2\text{R}$	$-\text{O}^-$
$-\text{NO}_2$	$-\text{F}$	$-\text{CR}=\text{CH}_2$	$-\text{CHR}_2$	$-\text{NH}^-$
$-\text{C}\equiv\text{N}$	$-\text{Cl}$	$-\text{CR}=\text{CR}_2$	$-\text{CR}_3$	
$-\text{COOH}$	$-\text{Br}$	$-\text{C}\equiv\text{CH}$		
$-\text{COOR}$	$-\text{OR}$			

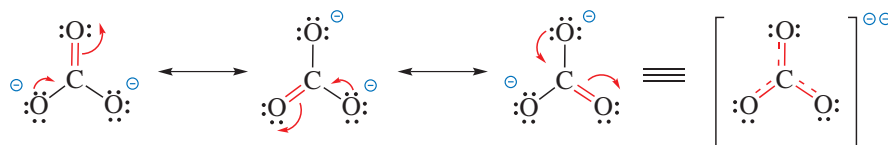
As can be seen in the Table 1.4, almost all other substituents, apart from the alkyl groups, are inductively electron-attracting groups ($-I$ effect) because they are more electronegative than the hydrogen atom is. Carbon-carbon double bonds and carbon-carbon triple bonds are also inductively electron-attracting groups. The σ bonds of these groups are formed by overlap of sp^2 and sp hybrid orbitals. Because the s ratio in these orbitals is higher than the ratio in sp^3 hybrid orbitals, they attract the electrons more. Alkyl groups are generally electron-donating groups ($+I$ effect). In the carboxylate anion, the carbonyl group is not an electron-attracting group because the electron density on the carbon atom is increased. Negatively charged oxygen and nitrogen atoms also lose their electron-withdrawing properties and become electron donors.

Functional groups such as aldehyde and ketones are inductively electron-attracting groups. When the resonance structures of these groups are drawn, it is seen that a positive charge is created on the carbon atom. Because carbonyl carbon is positively charged, it attracts the neighboring σ bond electrons. This behavior of the carbonyl group makes the carbonyl groups inductively electron attracting.

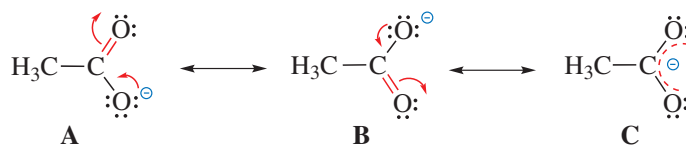
1.4.2 Mesomeric Effect (Resonance Structures)

Before describing the mesomeric effect, let us introduce the resonance structures of compounds. When a compound can be represented by more than one Lewis structure, the compound is said to possess resonance. If there are multiple double bonds in organic compounds and they are conjugated, double-bond electrons can change their position within the molecule. If there are nonbonded electrons adjacent to double-bond electrons, they also participate in conjugation. To clarify the issue, consider the Lewis structure of the carbonate ion, CO_3^{2-} , and acetate ion.

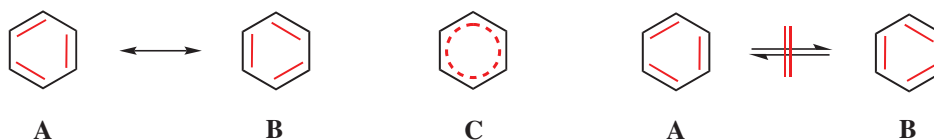
The carbonate anion has three oxygen atoms attached to the carbon atom. The Lewis structure for this ion has a carbon–oxygen double bond (C=O) and two carbon–oxygen single bonds (C–O). Each of the single bonded oxygen atoms bears a formal charge of -1 . We know that single and double bonds have different bond lengths and a double bond is shorter than a single bond. All three carbon–oxygen bond lengths in the carbonate ion have been shown experimentally to be equal. Moreover, all three oxygen atoms bear equal amounts of negative charge. However, we cannot write a Lewis structure that shows that these three bonds are equal. Under these circumstances, the concept of resonance has to be used. This indicates that the electrons are delocalized over four atoms and the molecule is resonance stabilized if two or more resonance structures can be drawn. The carbonate anion is actually a hybrid structure consisting of three resonance structures.



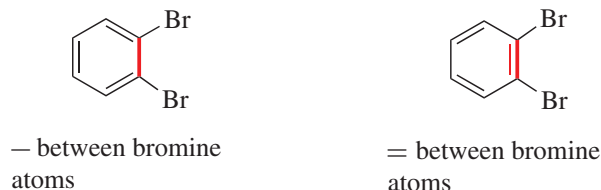
There is a similar situation in organic acids. Accordingly, one of the oxygen atoms is bonded with the double bond to the carbon atom and the other with a single bond. The distance between carbon and oxygen atoms should be different. Experimental and spectroscopic findings show that these two oxygen atoms are equivalent. Therefore, structures A and B do not show the true structure of the acetate ion. The true structure of the acetate ion is something between these two structures. The negative charge ($-$) and the π electrons are evenly distributed on the two oxygen atoms. This is also called resonance and the two individual line-bond structures for the acetate ion are called resonance forms. The actual structure is shown by C. In similar cases, if there are two or more resonance structures, the resonance relationship is indicated by a double-headed arrow (\leftrightarrow) between them. It is wrong to place two arrows (\rightleftharpoons) between the resonance structures. Two arrows indicate balance.



Electrons can delocalize over many atoms. Let us examine the structure of benzene. For example, structures A and B of benzene shown below do not reveal its true structure.



If the benzene structure with alternating single and double bonds had been correct, there would have been two different isomers of 1,2-disubstituted benzene derivatives. For example, the isomers of 1,2-dibromobenzene should be different according to the carbon-carbon bonds between the bromine atoms.

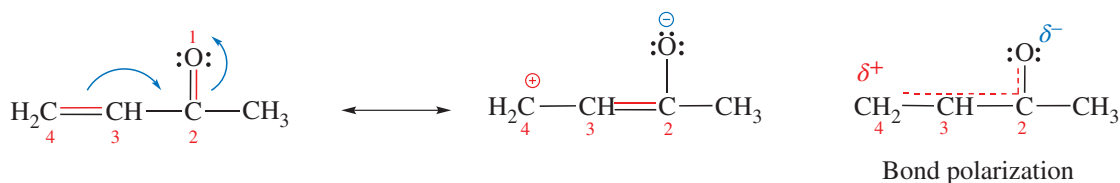


However, spectroscopic investigations at very low temperatures showed that there are not two different structures. Experimental studies, especially those employing X-ray diffraction, showed that benzene has a planar structure with equal C—C distances of 1.39 \AA , which is shorter than that of a carbon–carbon single bond (1.54 \AA) but longer than that of a C=C double bond (1.34 \AA). In other words, benzene does not have alternating single and double bonds. These intermediate distances

are explained by electron delocalization. The carbon atoms in benzene are sp^2 -hybridized. The p orbitals from each carbon atom overlap to form a delocalized molecular orbital that extends around the ring, giving stability and decreased reactivity to the benzene ring. To reflect the delocalized nature of the electrons, benzene is often depicted by a circle inside a hexagonal arrangement of carbon atoms as shown above. π Electrons are not localized in benzene but are distributed evenly over six carbon atoms. The distribution of electrons in the benzene molecule is a resonance (mesomer) event, not a valence isomerization. The real structure of benzene should be shown by C.

From what we have seen so far, we come to the following conclusion. π Electrons and nonbonding electrons in conjugated systems can be distributed through p orbitals over the system. As a result of the distribution of electrons on the molecule, charge polarization can occur, which is extremely important for the reactions.

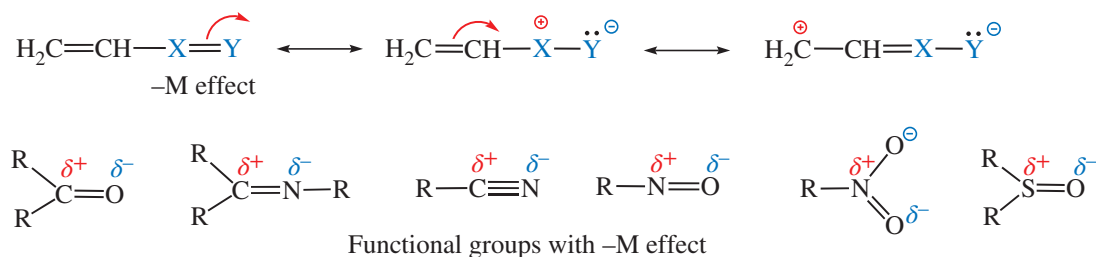
Let us examine the resonance process in another system. In the α,β -unsaturated carbonyl compounds, the C=C double bond, and the C=O double bond are separated just by one C—C single bond. This indicates that the double bonds are conjugated. Because oxygen is more electronegative in the C=O bond, electrons are withdrawn toward the oxygen atom and oxygen is negatively ($-$) charged. Because carbonyl carbon is positively ($+$) charged, it attracts the neighboring π electrons. Thus, the double bond between the carbon-carbon bond changes place. The structures shown below are resonance structures. Conjugation of a double bond to a carbonyl group transfers the electrophilic characteristic of the carbonyl carbon to the β -carbon atom of the double bond. According to this polarization, while the β -carbon atom becomes electrophilic, the oxygen atom becomes nucleophilic. The polarized structure thus formed determines the chemistry of the α,β -unsaturated carbonyl compounds. For example, nucleophiles attack the C4 carbon atom, while electrophiles bind to oxygen. Therefore, in order to decide where reagents will attack in a chemical reaction, we need to know the bond polarization within the molecule, in other words, the charge distribution.



The most important difference between the mesomeric effect and the inductive effect is that with the latter, σ electrons are pulled or pushed, so that the electron density is shifted toward the more electronegative atom and it is a permanent effect. With the mesomeric effect, π electrons are pulled or pushed through p orbitals. In the inductive effect, bond electrons do not change their position; they are only polarized. In the mesomeric effect, π electrons change their positions. Of course, the system must be conjugated. Nonbonding electrons can also be involved in the mesomerism. For this, the nonbonding electrons must be conjugated with the double bonds. The mesomeric effect can be categorized as "negative" and "positive" based on the properties of the substituent. The mesomeric effect is positive ($+M$) when the substituent is an electron-donating group and negative ($-M$) when the substituent is an electron-withdrawing group.

Now let us return to the α,β -unsaturated carbonyl compound we reviewed above. With carbonyl group polarization, the π -electrons of the double bond are attracted and the electrons change position. The double-bond electrons are shifted between the C2 and the C3 bond. Here, the mesomeric effect of the carbonyl group is negative ($-$).

It is extremely simple to determine whether the mesomeric effect of any functional group is $+M$ or $-M$. Suppose that there is a double bond or triple bond between X and Y ($-X=Y$ or $-X\equiv Y$) that is conjugated with a carbon-carbon double bond or an aromatic system. If atom Y is more electronegative than atom X, double-bond electrons will be withdrawn by the electronegative element Y. As a result, element X will be positively ($+$) charged and it will withdraw the conjugated double-bond electrons mesomerically toward it. In this case, the mesomeric effect of this functional group, $-X=Y$, will be $-M$. Almost all of the double bonds in organic chemistry have a $-M$ effect.

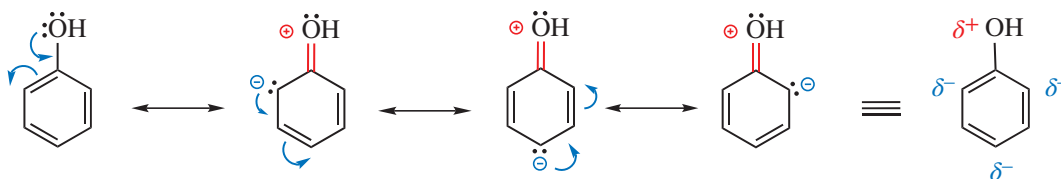


Functional groups with +M mesomeric effects are usually heteroatoms with nonbonding electrons. When these groups are directly attached to a double bond or aromatic ring, they act as electron-donating groups based on the resonance structures. Let us examine the behavior of an oxygen atom attached to the aromatic ring and how it affects the reactivity of the group to which it is attached.



Functional groups with +M effect

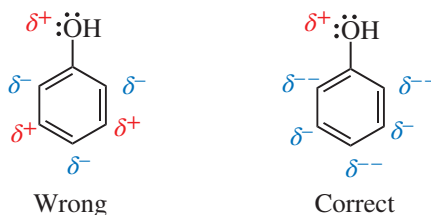
The resonance structures of phenol are studied in detail in basic organic chemistry courses. There are very important points that we need to emphasize here. As is known, oxygen is an electronegative atom that attracts electrons inductively (through σ bonds).



Resonance structures for phenol

In contrast to this behavior, oxygen donates nonbonding electrons to the aromatic ring. These electrons are delocalized over the benzene ring. Oxygen has performed an electron-donating task here. One of the most serious mistakes made by students is that they always perceive oxygen as an electron-withdrawing atom because of the electronegativity of oxygen. As can be seen here, oxygen not only attracts electrons but it also donates them to the conjugated systems. In that case, *the oxygen atom is an inductively electron-attracting ($-I$) mesomeric electron donor ($+M$)*. In this system, while the oxygen atom donates its nonbonding electrons to the ring, it draws electrons from the ring through the σ electrons. *What happens if an atom draws electrons inductively at the same time as it does here and donates the electrons mesomerically? The mesomeric effect, in most cases, dominates.* We have seen that the inductive effect is observed up to a maximum of three to four bonds. With the mesomeric effect, because electrons move and change their location, it takes place at longer distances. There are four bonds between the *para* position of phenol and oxygen. The electron density is high at the *para* position.

It is necessary to pay particular attention to one point. In order for the electron donor feature of oxygen to come to the fore, it must be connected to a conjugated system. The oxygen atom in phenol increases the electron density at the ring by donating its electrons to the benzene ring. The resonance structures of phenol show that the electron density at the *ortho* and *para* positions is increased. This does not mean that the electron density at the *meta* position is decreased. The electron density is increased around the entire benzene ring. However, the increase in density at the *meta* position is not as much as that at the other positions. In that connection, we can understand why the electrophiles exclusively attack the *ortho* and *para* positions of phenol. For more information, see Chapter 6. To illustrate this situation on the figure, the structure given below on the left is incorrect. The drawing on the right expresses the true structure.

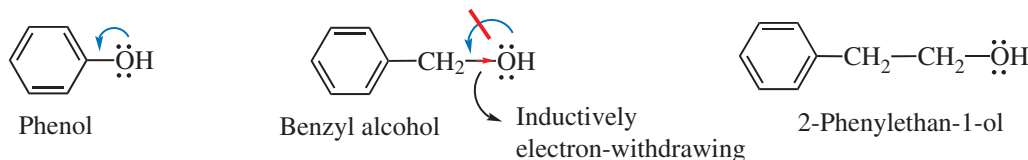


Phenol is potentially more reactive toward electrophilic substitution reactions than benzene is because the hydroxyl group strongly activates the benzene ring by electron donation. Then, the electrophiles attack the region with higher electron density.

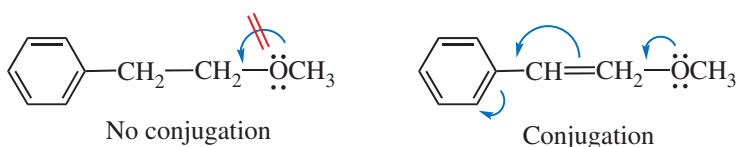
NMR spectroscopy gives accurate information about the electron density within a molecule. The chemical shifts are mainly affected by electron density. In the ^1H -NMR spectrum of phenol, the resonances of all aromatic protons are shifted to a higher field compared to benzene. This is due to the increased electron density in the aromatic ring. The *ortho* and *para*

protons are more affected than the *meta* protons are as expected from the resonance structures of phenol. Thus, we can draw the following conclusion: $^1\text{H-NMR}$ chemical shifts of substituted benzenes largely depend on the mesomeric interaction between the substituent and the benzene ring.

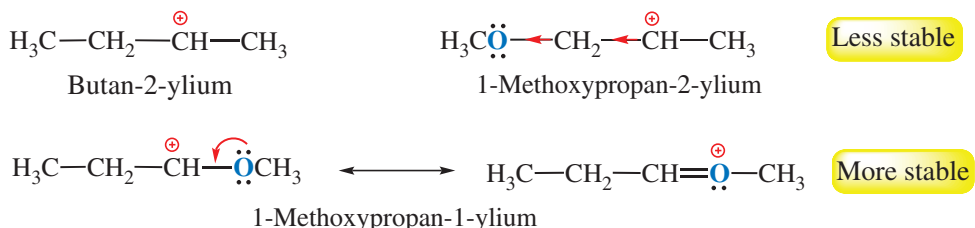
Let us examine the relationship between the mesomeric effect and the inductive effect on benzyl alcohol. In benzyl alcohol, a methylene group ($-\text{CH}_2-$) separates the hydroxyl group ($-\text{OH}$) from the benzene ring. *How does oxygen act here and how does it affect the electron density on the benzene ring?*



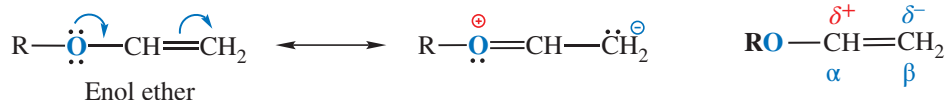
The nonbonding electrons of the oxygen atom cannot conjugate with the benzene ring because the conjugation is interrupted by the methylene ($-\text{CH}_2-$) group. Thus, the oxygen atom cannot donate electrons to the ring by resonance. However, oxygen inductively attracts the σ electrons and to a lesser extent reduces the electron density on the benzene ring. If an additional methylene group ($-\text{CH}_2-$) is added to benzyl alcohol, this time the inductive effect of oxygen will not be observed on the benzene ring. However, if the ethylene group is replaced by a $\text{C}=\text{C}$ double bond, now oxygen can deliver electrons to the benzene ring via resonance because of the uninterrupted conjugation.



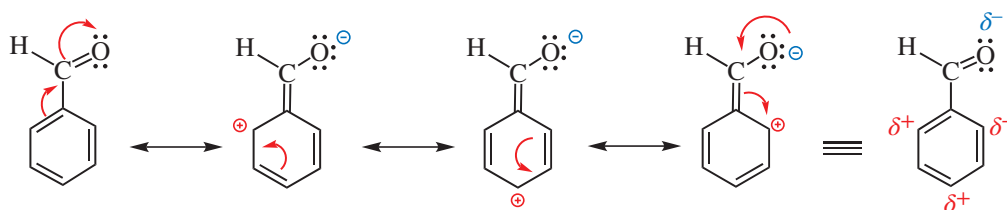
Let us examine the inductive and mesomeric effects of the oxygen atom on another system. The secondary butyl carbocation is more stable than the primary butyl carbocation. *How will the stability of this carbocation be affected if we replace the methyl group far from the carbocation center with an OCH_3 group?* Because the oxygen atom is not directly connected to the carbocation center, the nonbonding electrons on the oxygen atom cannot conjugate with the carbocation because the conjugation is interrupted by the methylene group. In this case, only the inductive effect of oxygen will occur, so the stability of the carbocation will decrease, because of the electron-withdrawing effect of the oxygen atom. If the oxygen atom is directly attached to the carbocation center, the stability of the carbocation will increase. Actually, oxygen will decrease the stability by attracting σ electrons more strongly. On the other hand, the nonbonding electrons on oxygen will conjugate with the empty p orbital located in the carbocation center. In other words, the oxygen atom releases its electrons mesomerically and withdrawing inductively. In cases where both effects occur simultaneously, the oxygen atom will make the carbocation more stable in the α -position, as the mesomeric effect is the dominant one.



For a better understanding of the subject, let us examine enol ethers, in which oxygen is directly attached to a double bond. First, it might be thought that oxygen will attract electrons from the double bond. This is true. However, while the oxygen atom inductively withdraws electrons, it releases its nonbonding electrons by resonance as we discussed in the case of phenol. Because the mesomeric effect is dominant, the electron density in the double bond increases. However, this increase is concentrated on the β -carbon atom. The positive charge is located on the oxygen and α -carbon atom. The $^1\text{H-NMR}$ spectra of enol ethers show this charge distribution well. The chemical shift value of the α -proton shifts approximately 1 ppm to a lower field, while the chemical shift value of the β -proton shifts 1 ppm to a higher field. The difference in the chemical shift of these protons is about $\Delta\delta = 2$ ppm, revealing serious electron polarization of the double bond. Again, NMR shows the bond polarization clearly. If this polarization is known, it is extremely easy to understand the chemistry of enol ethers. Enol ethers react easily with electrophiles. Because the electron density on the β -carbon atom is increased, electrophiles attack the β -carbon atom and open the carbon-carbon double bond. Therefore, enol ethers are extremely sensitive to acids.

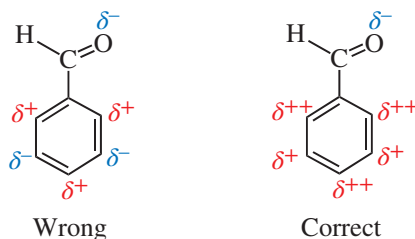


Let us analyze the effect of an electron-withdrawing group attached to benzene, for example, benzaldehyde. Because oxygen withdraws the electrons toward itself, the carbonyl group is polarized. Thus, the aldehyde is a group with a $-M$ effect. The polarized carbonyl carbon will withdraw the π electrons from the aromatic ring. Thus, electron delocalization occurs in the ring. The resonance structures of benzaldehyde are shown below. These structures show that the electron density at the *ortho* and *para* positions is decreased. This does not mean though that the electron density at the *meta* position is increased. The electron density is decreased around the entire benzene ring. However, the decrease in electron density at the *meta* position is not as great as that at the other positions. The $^1\text{H-NMR}$ spectrum of benzaldehyde also demonstrates the electron density distribution on the benzene ring. Comparison of the chemical shifts of the aromatic protons of benzaldehyde with those of benzene clearly indicates that the resonances of all protons are shifted to a lower field because of the decreased electron density at the benzene ring. The *meta* positions are less affected.

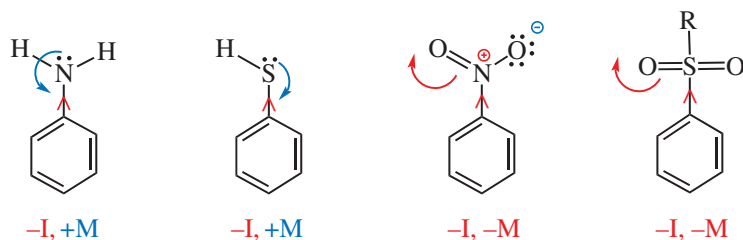


Resonance structures of benzaldehyde

Aromatic compounds, having substituents with a $-M$ effect, undergo electrophilic substitution reaction at the *meta* position. Such compounds generally undergo more difficult electrophilic substitution reactions than benzene does. The reaction conditions must be changed relative to benzene (high temperature, strong catalyst, etc.). Therefore, electron-withdrawing groups direct the electrophiles to the *meta* position because the *meta* positions have less positive charge as shown below.



In the examples provided above, we have examined oxygen-containing functional groups. For example, aniline behaves exactly like phenol. Although the amine group is an inductively electron-attracting group, it is mesomerically electron donating, so that the nonbonding electrons on the nitrogen atom can be involved in the resonance with the π electrons of the ring. Aromatic amines increase the electron density in the benzene ring. If sulfur atoms are directly attached to the ring such as $-\text{SH}$ or $-\text{SR}$, they behave similarly because they can easily donate the nonbonding electrons to the benzene ring. If nitrogen or sulfur, directly attached to the ring, contains a double bond with oxygen, the situation changes. Now, functional groups such as $-\text{NO}$ or $-\text{SO}-$ will attract the ring electrons inductively as well as mesomerically as shown below.

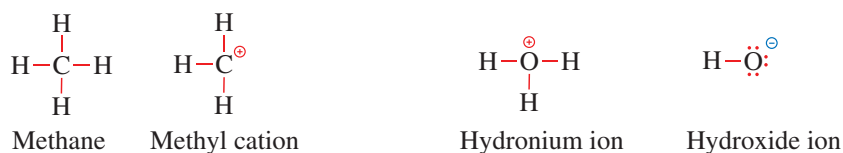


Inductive and mesomeric effects should always be considered jointly. It is now an easy process to predict how electron polarization will be in a molecule through these two effects. Once polarization is known, it is much easier to predict reactions because in all reactions, electron-rich functional groups attack the electron-deficient positions. Thus, knowing polarization is often enough to predict products that can occur as a result of a reaction. This subject will be frequently touched upon in the following chapters.

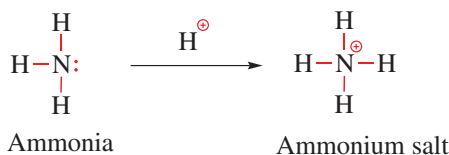
1.5 Formal Charge and Oxidation Number

1.5.1 Formal Charge

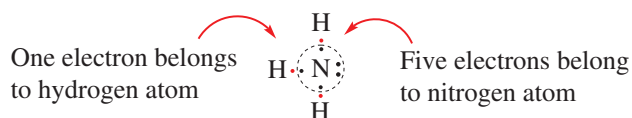
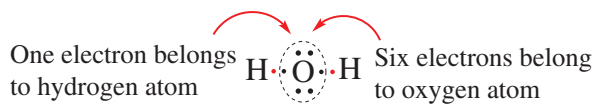
Most organic compounds are represented by Lewis structures having the normal number of bonds. On the other hand, some organic ions or molecules contain less than the customary number. For example, the carbon atom in methane contains four bonds (eight electrons) and methane does not have a charge. However, the carbon atom in the methyl cation has fewer bonding electrons (six electrons) and has a charge. The H_2O molecule forms a hydronium ion by treatment with acids. On the oxygen atom, there is a positive charge. If we remove a proton from water, a hydroxide ion will be formed, which has a negative charge on the oxygen atom. As one can see, in organic compounds or ions, there are some charges that are assigned to an atom in a molecule. These positive (+) and negative (-) charges do not show the oxidation number like they do in inorganic chemistry.



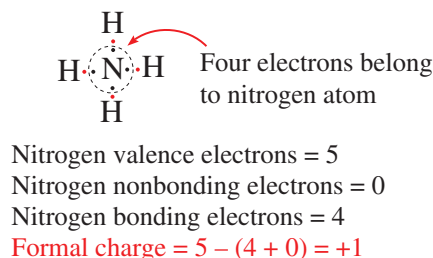
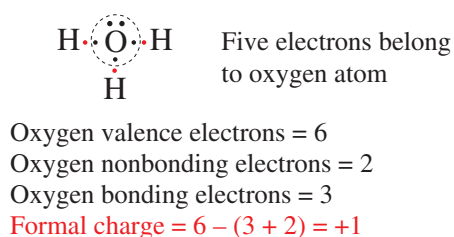
Ammonia is a neutral molecule. If it reacts with a mineral acid, an ammonium salt is formed. The molecule gains a positive (+) charge, which is assigned to the nitrogen atom. All these charges do not show the oxidation number of the corresponding atoms.



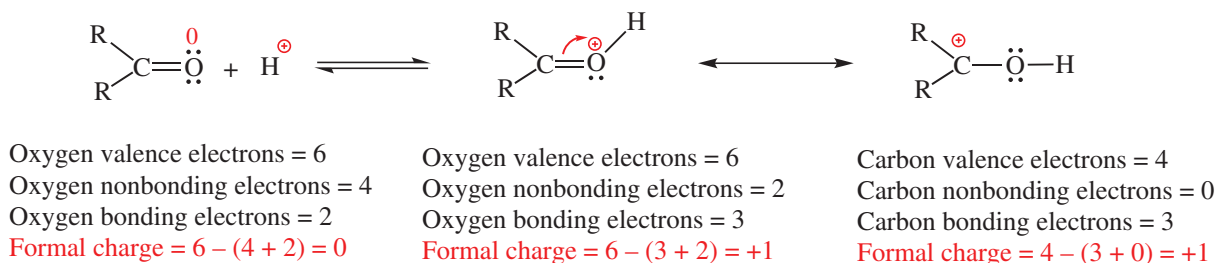
As we know, the oxidation numbers of oxygen in H_2O and nitrogen in NH_3 molecules are -2 and -3 , respectively. Furthermore, we know that protonation or proton abstraction of these compounds does not change the oxidation numbers. Then, we can ask: *What are these charges assigned to some atoms? How can we predict the charges?* These charges are called *formal charges*. *How is the formal charge of an atom calculated?* When calculating the formal charge of an atom, the electronegativities of other atoms attached to that atom are never taken into account. Formal charge is a hypothetical charge given to every atom in a molecule considering that the bonding electrons are shared equally between the atoms. Before starting to count the formal charge, first we determine how many valence electrons the corresponding atom has in the case where it is not bonded to any other atoms. In other words, we determine the group number of the atom in the periodic table. Half of the bonded electrons are assigned to each atom, irrespective of the electronegativities. Unshared electrons belong exclusively to the parent atom. Keeping this information in mind, let us calculate the formal charge of the oxygen and nitrogen atoms in H_2O and NH_3 molecules. As we see below, the oxygen atom in water has two pairs of nonbonding electrons. We divide all of the electrons in bonds equally between the atoms (hydrogen and oxygen) that share them. Thus, each hydrogen is assigned one electron. We subtract this number (one) from 1, which is the number of valence electrons in a hydrogen atom. The result is $(1-1=0)$ zero, which is the formal charge of hydrogen atoms in water. The oxygen atom is assigned six electrons (four nonbonding electrons + two shared electrons). We now subtract 6 from 6, which is the number of valence electrons in an oxygen atom to give the oxygen a formal charge of zero. The nitrogen atom in ammonia is assigned five electrons (two nonbonding electrons + three shared electrons). We subtract 5 from 5, which is the number of valence electrons of a nitrogen atom to give the nitrogen a formal charge of zero.



The formal charges of oxygen and nitrogen atoms in protonated H_2O and NH_3 molecules are shown below.



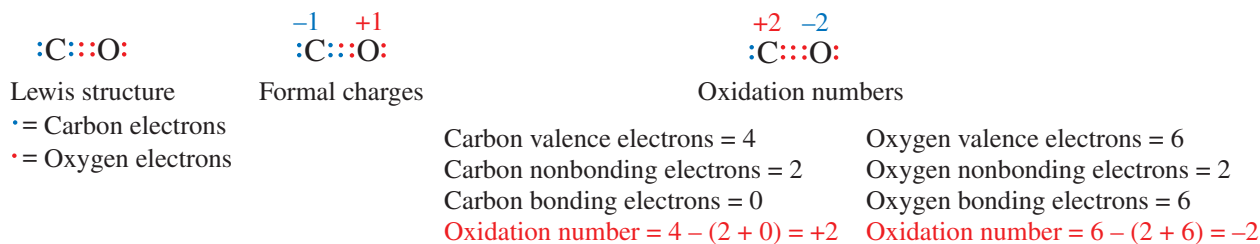
The acid-catalyzed reaction of carbonyl groups occurs by initial protonation of the nonbonding electrons of the carbonyl oxygen atom to produce resonance-stabilized intermediates. The carbonyl group contains a double bond between oxygen and carbon. Two of the four electrons belong to oxygen. We assign nonbonding electrons to oxygen. The oxygen atom now has six electrons, so that the formal charge of oxygen is zero. In the case of protonation, the oxygen atom has only two nonbonding electrons and the number of bonds made by oxygen becomes three. The number of electrons belonging to oxygen is now five. The formal charge of oxygen is then +1. In the resonance structure of the carbonyl group, the formal charge of oxygen is zero; however, the formal charge of the carbon atom changes from zero to +1.



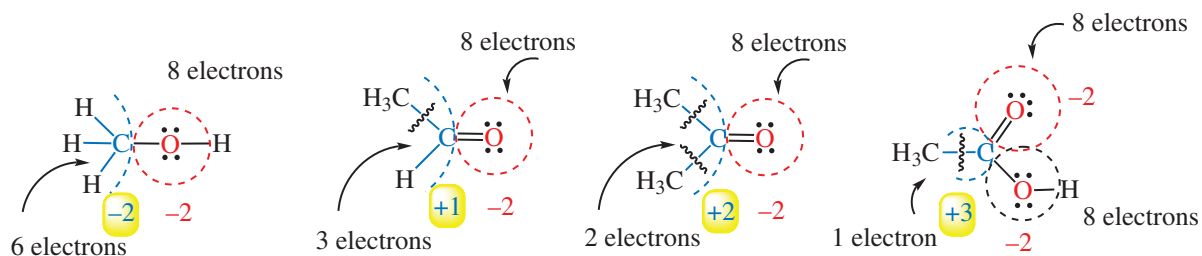
1.5.2 Oxidation Number

The oxidation number is another way of characterizing atoms in molecules. Let us try to determine the oxidation numbers after the formal charge calculation. The process is very similar. In contrast to the formal charge, in which the electrons in a bond are assumed to be shared equally, the oxidation number is a charge that an atom would have if the bonding electrons were assigned exclusively to the more electronegative atom.

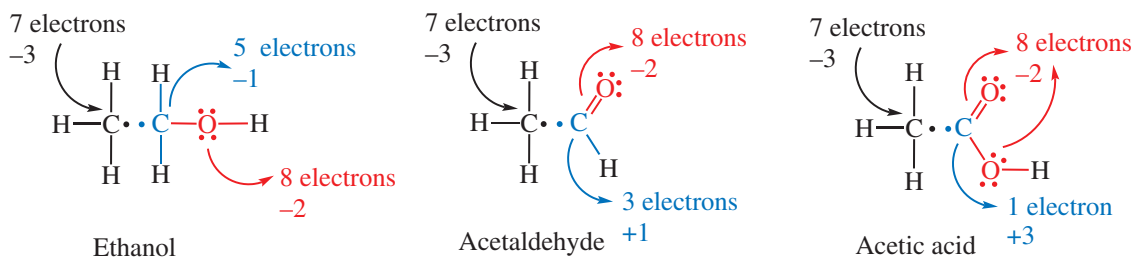
The following diagram compares the formal charge and oxidation numbers in carbon monoxide. The formal charges of the carbon atom and oxygen atom are calculated as -1 and $+1$, respectively, because the bonding electrons are equally shared between the carbon atom and oxygen atom. In the case of calculating the oxidation numbers, the bonding electrons are assigned to the more electronegative atom, which is the oxygen atom. Then, the oxygen atom has eight electrons in the outer shell and its oxidation number is -2 . The oxidation number of the carbon atom is calculated as $+2$.



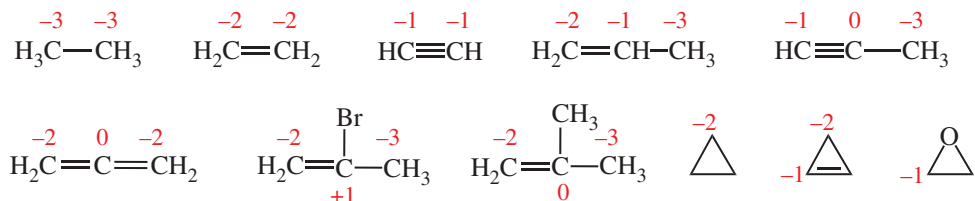
Various functional groups such as alcohol, ketone, aldehyde, and carboxylic acid are formed as a result of bonding between the carbon and oxygen atoms. Let us calculate the oxidation numbers of carbon and oxygen atoms in these functional groups. As seen below, the oxidation number of the oxygen atom in all of these groups is -2 . However, the oxidation number of the carbon atom varies according to the number of bonds between the carbon and the oxygen atom.



If there are one or more bonds between two carbons, due to the same electronegativity, half of the bond electrons belong to one carbon atom and half to the other. We can easily find that the oxidation number of one of the carbon atoms of ethanol is -3 and that of the other is -1 .

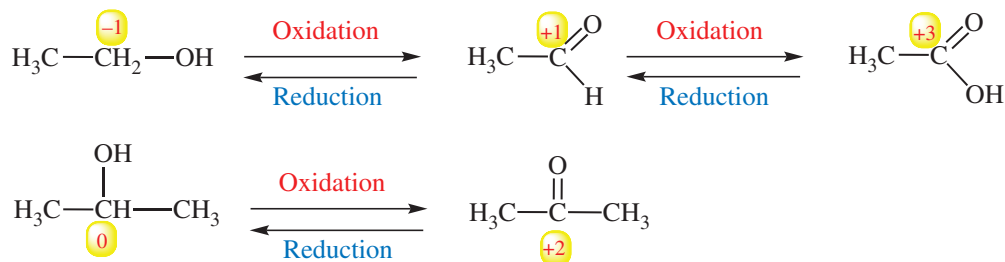


The oxidation numbers of carbon atoms in an unsaturated carbon chain can vary. For example, the oxidation numbers of carbon atoms in different compounds are given below.

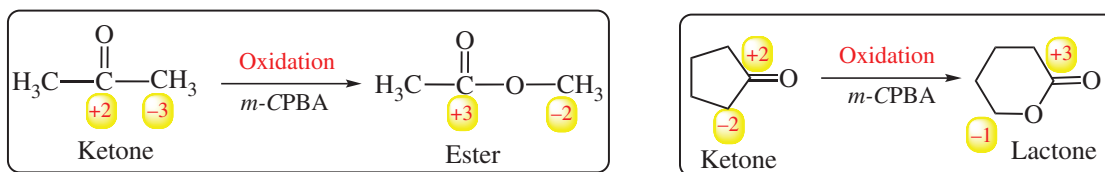


After examining the oxidation numbers of carbon atoms at various positions, let us briefly examine the oxidation and reduction phenomena in organic chemistry. In inorganic chemistry, it is easy to determine whether there is oxidation or reduction during a reaction as the oxidation numbers of the elements are always given. Because formal charges are generally used in organic chemistry, students often have difficulty determining the reduction and oxidation reactions. Occasionally, these reactions are confused with hydrolysis reactions. This confusion must be resolved before starting with the mechanism. Let us start with the simple examples known.

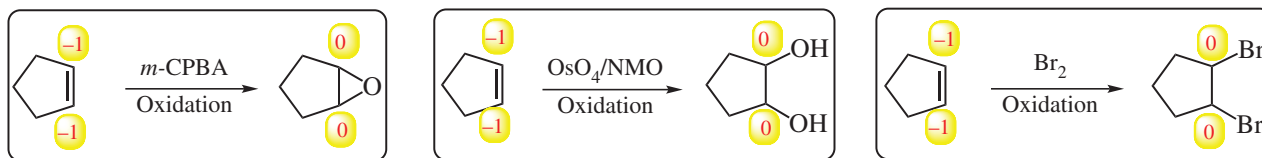
Conversion of ethanol to acetaldehyde is an oxidation reaction as presented. The oxidation number of the carbon atom bearing the hydroxyl group increases from -1 to $+1$. Conversion of aldehyde to a carboxylic acid is also an oxidation reaction. Here, the oxidation number of the carbon atom increases from $+1$ to $+3$. The reverse reactions, of course, are reduction reactions. The conversion of a secondary alcohol to a ketone is an oxidation reaction because the oxidation number of the carbon atom changes from 0 to $+2$. Therefore, we have to use oxidizing reagents such as permanganate and chromate to perform this reaction.



The Baeyer–Villiger oxidation, the reaction of ketones with *m*-chloroperbenzoic acid, is an oxidative cleavage of a carbon–carbon bond adjacent to a carbonyl group, which converts ketones to esters and cyclic ketones to lactones. To understand whether these reactions are redox reactions, it will be sufficient to examine the oxidation numbers of the carbon atoms reacted. In straight-chain ketones, the carbonyl group is oxidized from +2 to +3 and the carbon atom to which oxygen bonded is oxidized from –3 to –2. In cyclic ketones, carbonyl carbon is oxidized from +2 to +3 and the other carbon atom from –2 to –1.



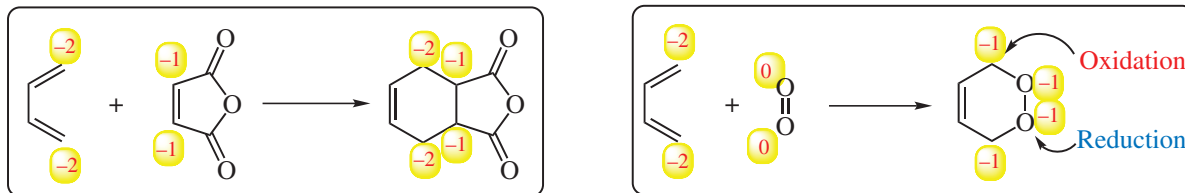
Alkenes usually undergo electrophilic addition reactions at carbon–carbon double bonds and the π bond is removed and two new σ bonds are formed. Let us examine these reactions in terms of oxidation and reduction. Epoxidation of double bonds is a very common reaction applied in organic chemistry. As you can see, the oxidation numbers of the double-bond carbon atoms both change from –1 to 0, which is an oxidation reaction. The hydroxylation reaction of the double bonds is also an oxidation reaction. Here, double-bond carbon atoms are also oxidized from –1 to 0, while OsO_4 is reduced. It may not be possible to see in the first stage that the bromination reaction, which is one of the most common and classic reactions in organic chemistry, is also an oxidation reaction. However, when we look at the oxidation numbers of the carbon atoms to which bromine is added, it is immediately understood that they are oxidized from –1 to 0, as in epoxidation and hydroxylation reactions.



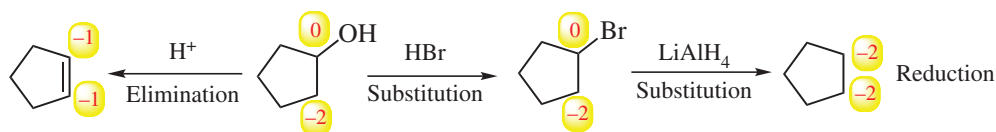
Cleavage of carbon–carbon bonds is usually an oxidation reaction. Of course, the electronegativity of the element that will be attached to the carbon atom after the cleavage will determine this. Generally, in organic chemistry, as elements other than hydrogen are more electronegative than carbon, the carbon–carbon cleavages are oxidation reactions.



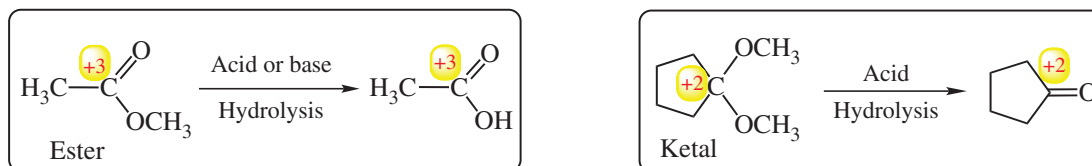
Are Diels–Alder reactions redox systems? To answer this question, we need to look at the oxidation numbers of the reacting carbon atoms. For example, the cycloaddition reaction of butadiene with maleic anhydride is neither oxidation nor reduction because the oxidation numbers of the starting materials are not changed. However, if the dienophile is an oxidizer, the diene can be oxidized. For example, the reaction of singlet oxygen with butadiene results in the formation of monocyclic endoperoxide. The carbon atom to which oxygen is bonded is oxidized and oxygen itself is reduced.



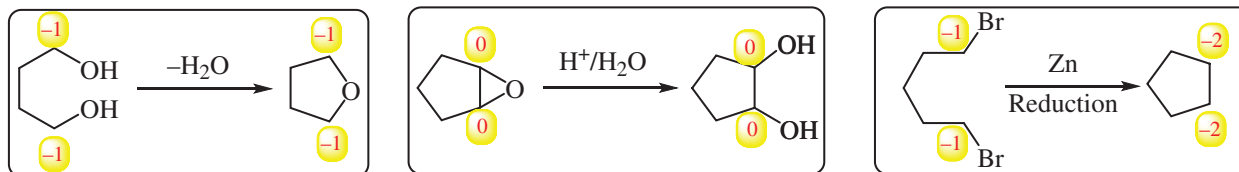
Elimination of H_2O from alcohols is a simple way to generate a double bond. The oxidation number of the carbon atom to which the hydroxyl group is attached is 0, and the oxidation number of the carbon atom from which the proton is removed is -2 . The oxidation numbers of double-bond carbons formed as a result of elimination are -1 . Here, while one of the carbon atoms is oxidized, the other is reduced. Substitution of the hydroxyl group with a bromide ion forms the corresponding brominated compound. As bromine and oxygen atoms are more electronegative than carbon atoms, there is no change in the oxidation number of carbon atoms. However, if the bromide atom is substituted with an element with a smaller electronegativity than the carbon atom, such as the hydride (H^-) ion, then the carbon atom is reduced. Here, the oxidation number of the carbon atom changes from 0 to -2 .



After examining the oxidation and reduction in many different reactions, let us take a brief look at the hydrolysis reactions where students become confused. Hydrolysis of esters in an acidic or basic medium is the conversion of esters to carboxylic acid and alcohol by addition of water to the medium. There is no change in the oxidation numbers of carbon atoms in ester hydrolysis. Thus, hydrolysis of a ketal to a ketone is also a reaction without oxidation or reduction.



Cyclization reactions such as conversion of diols to cyclic ethers or ring opening of an epoxide ring to give diols are not oxidation or reduction reactions. The oxidation numbers of the carbon atoms do not change. However, Wurtz-type reactions are reduction reactions.



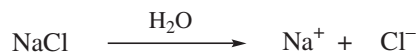
1.6 Acids and Bases

All chemical reactions are acid–base reactions. In order to predict what kind of product will be formed as a result of a chemical reaction, we have to know the acid and base properties of the functional groups in the reactants. For this reason, the concepts of acids and bases must be understood well. There are different descriptions for acids and bases. We will examine acids and bases in four different ways.

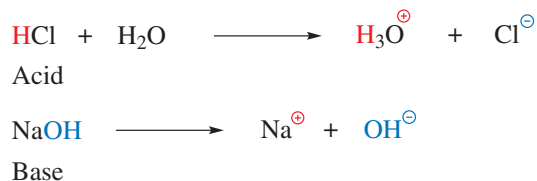
- Arrhenius theory
- Brønsted–Lowry theory
- Lewis theory
- Pearson hard–soft acid–base (HSAB) theory

1.6.1 Arrhenius Acid–Base Theory

The Arrhenius acid–base theory [1, 2] is the most classical theory. In 1884, Arrhenius suggested that NaCl dissociate when they dissolve in water to give particles and he called these particles ions.



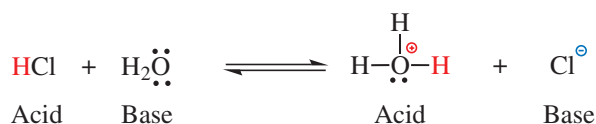
Shortly after this, he extended his theory to acids and bases. According to his theory, an Arrhenius acid is a substance that dissociates in water to form hydrogen ions (H^+) and protonation of water yields the hydronium ion, H_3O^+ . An Arrhenius base is a substance that dissociates in water to form hydroxide (OH^-) ions. In 1903, Svante August Arrhenius (1859–1927) received the Nobel Prize in Chemistry for his electrolytic dissociation theory of acids, bases, and salts.



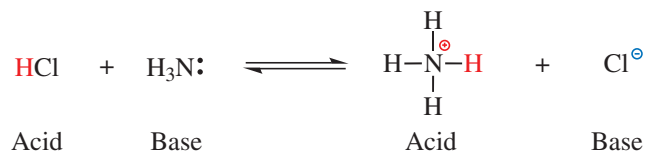
According to the International Union of Pure and Applied Chemistry (IUPAC) definition, H_3O^+ ions are called oxonium ions. Later, the IUPAC proposed calling these ions *hydronium ions*. The OH^- ions formed by bases are called *hydroxide ions*. The definition of Arrhenius acids and bases is a very classic definition but it has some limitations. For example, it is only applicable to compounds having the formula HX for acids and MOH (M = metal) for bases. This theory cannot be applied to explain the acidic properties of compounds such as AlCl_3 , CO_2 , and SO_2 as they cannot dissociate into H_3O^+ ions. In order for a molecule to be a base, it must be decomposed into hydroxide ions. This can only be created with metal hydroxides. Similarly, this theory cannot explain the basic properties of NH_3 , pyridine, Na_2CO_3 , etc. It also cannot explain the acidic and basic properties of HCl and NaOH in benzene or acetone or in the gaseous state. Therefore, we will not generally use the Arrhenius acid–base theory when studying organic reactions. This theory was later expanded by Brønsted and Lowry and interpreted to include a larger group.

1.6.2 Brønsted–Lowry Acid–Base Theory

According to the Brønsted–Lowry acid–base theory [3], an acid is a species that can donate a proton, H^+ (in accordance with Arrhenius theory), and a base is a species that can accept a proton, H^+ [4, 5]. For example, when hydrogen chloride dissolves in water, almost all of the molecules dissociate into the corresponding ions, which indicates that the products are favored at equilibrium and the equilibrium lies to the right. HCl is an acid because it donates a proton, H^+ . Water is a base because it accepts a proton from HCl. As water has two pairs of nonbonding electrons, it can form a covalent bond with a proton as shown below. When we examine this reaction from right to left, the H_3O^+ ion is an acid because the oxonium ion donates a proton, H^+ . The chloride ion, Cl^- , is a base because it accepts a proton.

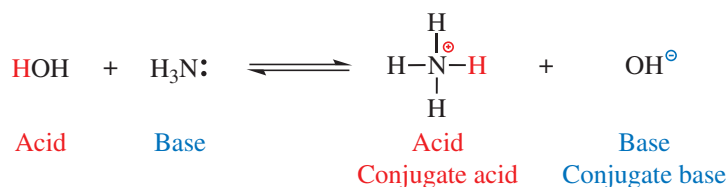


Let us examine the reaction between HCl and NH_3 . Here, ammonia (NH_3) is a base because it accepts a proton from HCl. The proton forms a covalent bond with the nonbonding electrons of the nitrogen atom in ammonia. When we examine the reaction from right to left, we can see that the ammonium ion (NH_4^+) is an acid and the Cl^- ion is a base. We can generalize the Brønsted–Lowry acid–base theory as follows. Species that have a hydrogen atom can potentially act as an acid and those possessing nonbonding electrons can potentially act as a base.



The concept of *conjugate pairs* is useful in describing Brønsted–Lowry acid–base reactions. When an acid donates H^+ , the remaining species is called its *conjugate base*. Thus, Cl^- is the conjugate base of HCl and H_2O is the conjugate base of H_3O^+ . Likewise, when a base accepts H^+ , the resulting species is called its *conjugate acid*.

In a reaction between water and ammonia, water is an acid because it donates a proton. Ammonia accepts this proton and therefore ammonia is a base. Thus, the NH_4^+ ion is the conjugate acid of NH_3 and the OH^- ion is the conjugate base of H_2O . The reaction between water and ammonia illustrates this idea. In the forward direction, water acts as an acid by donating a proton to ammonia and subsequently becoming a hydroxide ion, OH^- , the conjugate base of water. In the reverse reaction, a OH^- ion acts as a base in accepting a proton from the NH_4^+ ion, which acts as an acid.



It is possible to draw the following conclusion from the simple examples we have given above. Brønsted–Lowry acids turn into Brønsted–Lowry bases by giving protons, and Brønsted–Lowry bases turn into Brønsted–Lowry acids by bonding a proton. Important conjugate acid–base pairs are given below.

Acid	Conjugate bases	Bases	Conjugate acids
H_2SO_4	HSO_4^-	NH_3	NH_4^+
HCl	Cl^-	H_2N^-	NH_3
H_2O	HO^-	SO_4^{--}	HSO_4^-
H_2S	HS^-	H_2O	H_3O^+
NH_4^+	NH_3	NO_3^-	HNO_3
H_3O^+	H_2O	HPO_4^{--}	H_2PO_4^-

The Brønsted–Lowry acid–base theory has occasionally sparked controversy within the scientific community. Ideas have also been proposed to change the definition as follows. According to this theory, compounds that are capable of detaching protons are called acids, while compounds that can abstract a proton from another compound are called bases. Not every compound can easily donate protons, but if there are strong bases, then a proton can be abstracted.

For example, acetylacetone is not a compound that can donate a proton like HCl can. However, a strong base can easily abstract a proton from the methylene group between the two carbonyl groups to generate an anion. Therefore, we say that the methylene protons are acidic protons.



1.6.3 Lewis Acid–Base Theory

The Arrhenius acid–base theory [4] does not take into account the acid–base phenomenon in anhydrous environments. The Brønsted acid–base theory is very restrictive and focuses primarily on acids and bases acting as proton donors and acceptors. Furthermore, it completely eliminates compounds that do not have a proton. In 1923, G. N. Lewis (1875–1946) at UC Berkeley proposed an alternate theory: a *Lewis acid* is a species that accepts an electron pair and a *Lewis base* is a species that donates an electron pair [6]. According to this definition, a proton is a Lewis acid. This definition includes many compounds that do not contain protons. Through the use of Lewis' definition of acids and bases, chemists can now predict a wider variety of acid–base reactions.

Let us examine the reaction between a proton (H^+) and H_2O within the framework of the Lewis acid–base theory. Because proton is an electron-deficient species (Lewis acid), it can easily accept a pair of electrons. Oxygen (Lewis base), on the other hand, can form a new σ bond by transferring a pair of nonbonding electrons to the proton.



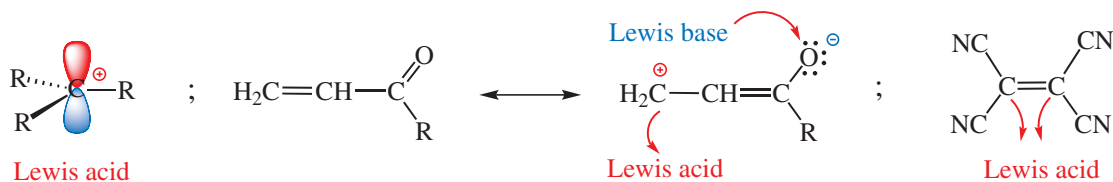
The Lewis acid–base theory explains why BF_3 reacts with NH_3 to form a complex. Boron trifluoride has a trigonal plane structure and its hybridization is sp^2 and it has an empty p orbital, which can accept electrons. According to the Lewis acid–base theory, boron trifluoride with six electrons in the outer shell is a Lewis acid. Ammonia consists of a nitrogen atom as the central atom with a pair of nonbonding electrons and so it is a Lewis base. The nonbonding electron pair from NH_3 is donated to the empty orbital of boron, forming a σ bond between the nitrogen and boron. As no proton (H^+) transfer is involved in this reaction, it qualifies as an acid–base reaction only according to Lewis' definition.



In the same way, AlCl_3 , a compound of third row elements, is a Lewis acid, because aluminum has a sextet of electrons in its outer shell. Similarly, many other compounds, such as ZnCl_2 , FeCl_3 , SnCl_4 , and TiCl_4 , are also Lewis acids.

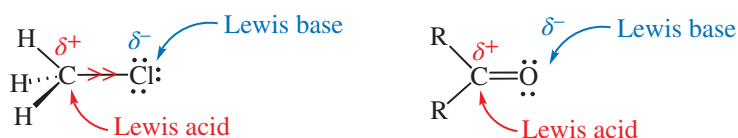


Carbocations also fall into the Lewis acid class. A carbocation, as seen earlier, has an empty p orbital. Carbocations are highly prone to bonding by accepting electrons from Lewis bases. Double bonds with low electron density, for example, enon-type compounds, accept electrons in the β -position and form a covalent bond. The double-bond carbon atoms of tetracyanoethylene also act like Lewis acids. Cyano groups reduce the electron density of the double bond because of their strong electron-withdrawing properties. The double bond can accept an electron pair from another compound and therefore such double bonds with electron deficiency are Lewis acids.



The hydride ion (H^-) is a typical Lewis base. It reacts easily with Lewis acids and forms a covalent bond. Nonpolarized double-bond electrons are also Lewis bases because of their high electron density. They can easily react with Lewis acids.

Polarized bonds form dipoles. One end of these bonds is a Lewis acid while the other end is a Lewis base. For example, a carbon–halogen bond is a polarized bond. Because the halogen atom attracts σ electrons between carbon and halogen more strongly and has nonbonding electrons, the halogen is a Lewis base. On the other hand, the carbon atom, whose electron density is reduced, acts as a Lewis acid. The carbonyl groups are polarized. Therefore, the carbonyl carbon atom is a Lewis acid and the carbonyl oxygen is a Lewis base.



1.6.4 Pearson Hard and Soft Acid–Base Theory

In 1963, Ralph Pearson first introduced the qualitative *theory of hard and soft acids and bases (HSAB)*, which initially included inorganic compounds and later organic compounds [5, 6]. According to this theory, Lewis acids and Lewis bases are divided into two classes: hard and soft.

Hard acids and hard bases tend to the following:

- Be small
- Have high oxidation state (the charge criterion applies mainly to acids and to a lesser extent to bases)
- Be difficult to polarize
- Have high electronegativity
- Have low-lying highest occupied molecular orbital (HOMO) energy (bases) and high-lying lowest unoccupied molecular orbital (LUMO) energy (acids).

Soft acids and soft bases tend to:

- Be large
- Have low or zero oxidation state
- Have high polarizability
- Have low electronegativity
- Have high-lying HOMO energy (bases) and low-lying LUMO energy (acids).

According to this theory, hard acids prefer to bind to hard bases, whereas soft acids prefer to bind to soft bases.

1.6.4.1 Hard Acids and Bases

Hard bases are characterized by low-energy HOMOs. Generally, the compounds derived from strong electronegative elements and their anions are hard bases. For example, because the central atoms of elements such as HO^- , F^- , Cl^- , and NH_3 are strongly electron withdrawing, HOMO energy levels are generally low. In the case of hard acids, LUMO energy levels are very high. Alkali metal cations (Li^+ to Cs^+), alkaline earth metal cations (Be^{2+} to Ba^{2+}), transition metal cations in higher oxidation states (Ti^{4+} , Cr^{3+} , and Fe^{3+}), and the proton (H^+) are hard acids. When hard acids react with hard bases, the strong bond formed between the acid and the base is usually an ionic bond. The large electronegativity differences between hard acids and hard bases give rise to strong ionic interactions.

When the energy gap between the orbitals participating in the reaction is very high, the probability of forming a covalent bond decreases. Because of the large energy gap between the atomic orbitals that will form molecular orbitals, the energy gain by forming molecular orbitals will be less, as depicted in Figure 1.21.

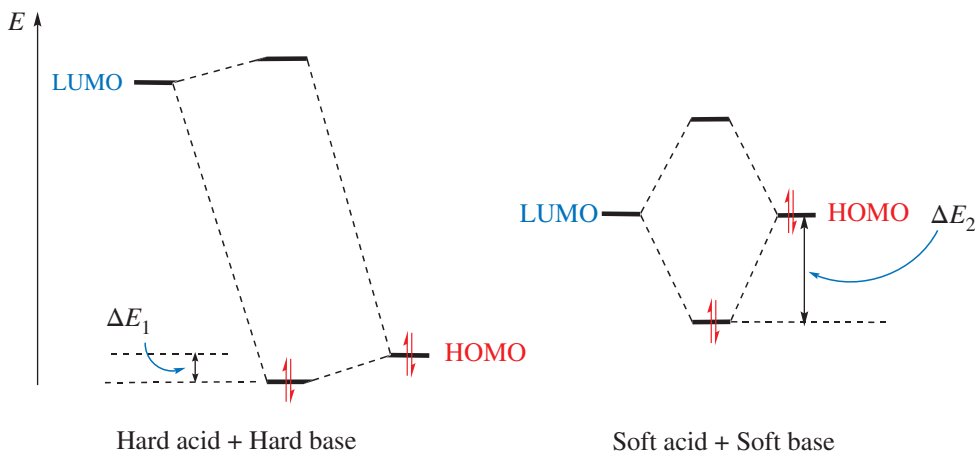


Figure 1.21 Formation of molecular orbitals by interaction of HOMOs and LUMOs with different energy levels and energy gain.

For example, let us examine the formation of a bond between Na and F atoms. In this reaction, the sodium atom loses its single valence electron to the fluorine atom, which accepts it. The ions produced are oppositely charged and are attracted to one another because of the electrostatic forces. If the two elements form a covalent bond, the energy level of the molecular

orbital will not drop so much because the energy difference between the HOMOs and LUMOs is quite large (Figure 1.21). Therefore, they cannot form a covalent bond.

1.6.4.2 Soft Acids and Bases

While the HOMO levels of soft bases are quite high, the LUMO levels of soft acids are low. When soft acids and soft bases react, they form a covalent bond. Because the energy levels of the orbitals (HOMO and LUMO) are close to each other, the energy levels of the formed molecular orbitals will drop. When the electrons settle into the bonding orbital, the energy released is high and the bond becomes strong (Figure 1.21). These compounds are easily polarized and their electronegativity is very weak. Some examples are given in Table 1.5 for HSAB.

Table 1.5 Examples of hard and soft acids and bases.

Type of acids and bases	Examples
Hard bases	H ₂ O, HO ⁻ , F ⁻ , Cl ⁻ , CH ₃ COO ⁻ , PO ₄ ³⁻ , SO ₄ ²⁻ , NO ₃ ⁻ , CO ₃ ²⁻ , ROH, RO ⁻ , R ₂ O, NH ₃ , RNH ₂ , N ₂ H ₄
Hard acids	H ⁺ , Li ⁺ , Na ⁺ , K ⁺ , Be ²⁺ , Mg ²⁺ , Ca ²⁺ , Al ³⁺ , Fe ³⁺ , Cr ³⁺ , Ti ⁴⁺ , Sn ⁴⁺ , Si ⁴⁺ , BF ₃ , B(OR) ₃ , AlCl ₃ , SO ₃ , RCO ⁺ , CO ₂ , R ₃ C ⁺
Soft bases	R ₂ S, RSH, RS ⁻ , I ⁻ , SCN ⁻ , PR ₃ , P(OR) ₃ , CN ⁻ , CO, CH ₂ =CH ₂ , C ₆ H ₆ , H ⁻ , R ⁻
Soft acids	Cu ⁺ , Ag ⁺ , Hg ⁺ , Pd ²⁺ , Hg ²⁺ , Pt ²⁺ , I ⁺ , Br ⁺ , RO ⁺ , I ₂ , Br ₂ , (CN) ₂ C=C(CN) ₂ , carbenes

In 1983, Ralph Pearson and Robert Parr [7] converted the qualitative definition of HSAB to a quantitative one by using the following equation. The chemical hardness is half the difference between the ionization potential (I) and the electron affinity A .

$$\text{Hardness} = \eta = \frac{1}{2}(I - A) \quad \text{Softness} = \sigma = 1/\eta$$

Ionization energy (I) is the minimum amount of energy required to remove the most loosely bound valence electron. Electron affinity (A) is the amount of energy released when an electron is attached to a neutral atom or molecule to form a negative ion.

Table 1.6 Chemical hardness of some atoms, acids, and bases.

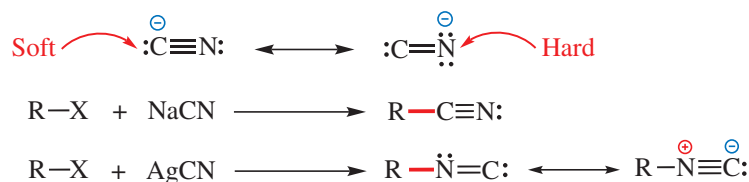
Atom	η	Cations	η	Anions	η
H	6.4	H ⁺	∞	H ⁻	6.8
Li	2.4	Li ⁺	35.1	F ⁻	7.0
C	5.0	Mg ²⁺	32.5	Cl ⁻	4.7
N	7.3	Na ⁺	21.1	Br ⁻	4.2
O	6.1	Ca ²⁺	19.7	I ⁻	3.7
F	7.0	Al ³⁺	45.8	CH ₃ ⁻	4.0
Na	2.3	Cu ⁺	6.3	NH ₂ ⁻	5.3
Si	3.4	Cu ²⁺	8.3	OH ⁻	5.6
P	4.9	Fe ²⁺	7.3	SH ⁻	4.1
S	4.1	Fe ³⁺	13.1	CN ⁻	5.3
Cl	4.7	Hg ²⁺	7.7		

Table 1.6 shows the chemical hardness of some selected atoms, acids, and bases. Hardness increases with electronegativity. The order for the halogens is F⁻ > Cl⁻ > Br⁻ > I⁻ and for the second-row anions is F⁻ > OH⁻ > NH₂⁻ > CH₃⁻. For cations, hardness increases with positive charge and decreases with size, so that H⁺ > Al³⁺ > Li⁺ > Mg²⁺ > Na⁺. The hardness of the proton is infinite as it does not have an electron. The Na⁺ ion is harder than the Ag⁺ ion because sodium has a smaller volume. The alkoxide ion RO⁻ is harder than the RS⁻ ion; because the oxygen atom is more electronegative, it increases the hardness. The Cu²⁺ ion is harder than Cu⁺. The increased oxidation number also increases the hardness.

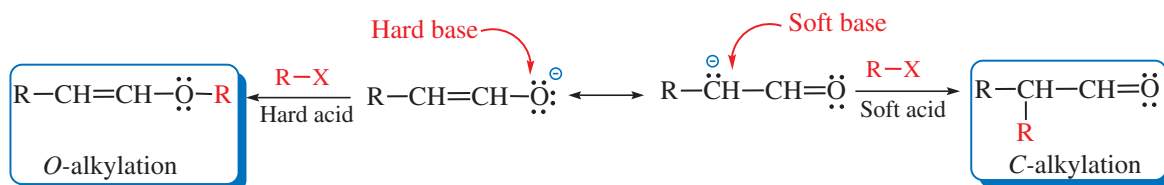
Let us try to apply the HSAB concept to some chemical reactions. Hard bases and hard acids generally form ionic compounds. There are always some exceptions. For example, HO⁻, which is a hard base, reacts with a hard acid, H⁺, to form

H₂O, where the bond between the hydrogen atom and the oxygen atom is a covalent bond. C=C double bonds are generally classified as soft bases. Because H⁺ is a hard acid, it does not react easily with double bonds. On the other hand, the bromonium ion, Br⁺, which is very soft, reacts quickly with double bonds to give addition products.

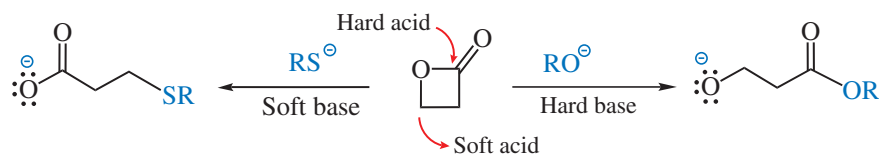
An ambident nucleophile is the one that can attack from two or more places, resulting in two or more products. An example of an ambident nucleophile is the nitrile ion, which has the chemical formula CN⁻. This ion can execute nucleophilic attacks from either the nitrogen atom or the carbon atom. The nucleophilic substitution reactions of alkyl halides involving this ion often result in the formation of a mixture of products. Therefore, an ambident nucleophile can be thought of as an anionic nucleophile in which the negative charge of the ion is delocalized by resonance over two different atoms. When the negative charge is on the nitrogen atom, the nitrile ion is much harder. The product distribution in the reaction of the CN⁻ ion with alkyl halides varies depending on the reaction conditions. When NaCN is used, the nitrile group is attached via carbon, and when AgCN is used, the nitrile group is attached to the alkyl group on nitrogen and isonitrile is formed (for a detailed discussion, see Section 2.1.6).



Enolate anions are nucleophiles and the negative charge on an enolate ion is delocalized over two atoms. Because of the nucleophilic characteristic of enolate anions, they can undergo alkylation reactions. Because of the enolate's ambident characteristic, *O*-alkylation or *C*-alkylation may take place. The question is which position in the enolate ion is a harder base. In alkylation with alkyl halides, if the electrophile is a soft acid, *C*-alkylation of the enolate is favored, because of carbon's lower hardness. Hard acids prefer the reaction of the enolate anion with the oxygen atom.



Oxetan-2-one can undergo ring-opening reactions with nucleophiles in two different ways. Nucleophiles can attack both the carbonyl group and the alkoxy carbon atom. Because the carbonyl group is more polarized and positively ($\delta+$) charged, it is a hard acid. The alkoxide anion, which is a hard base, attacks preferentially the carbonyl group and opens the β -lactone ring. On the other hand, thiolate is a soft base because of the sulfur atom and it attacks the alkoxy carbon atom, which has a soft acid property. Similar examples will be examined in more detail in the nucleophilic substitution section.

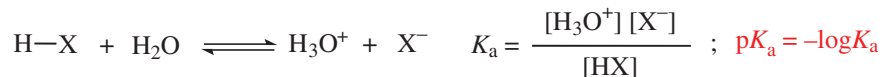


After examining different acid and base theories, in the next section, we will examine the pK values of acids and bases and the factors affecting the acid and base strength.

1.6.5 pKa Values of Acids

Many organic reactions involve the transfer of a proton (H⁺) by an acid–base reaction. Water is the reference solvent commonly used to compare the strengths of acids. When a strong acid H–X is dissolved in water, a proton is transferred from H–X to H₂O to form H₃O⁺ and X⁻. Almost all the molecules dissociate, which indicates that the products are favored. However, if a weak acid, such as acetic acid, is dissolved in water, very few molecules dissociate and so the reactants are favored. In both cases, an equilibrium will be established. A quantitative measure of the acidity is given by the equilibrium constant for

ionization, which is obtained from the following equation. Brackets are used to indicate the concentrations of all species, which are in equilibrium.



It is not appropriate to express the strengths of acids with K_a values. For convenience, the strength of an acid is generally expressed by its $\text{p}K_a$ values rather than its K_a values. The $\text{p}K_a$ values are the negative logarithm of K_a . The $\text{p}K_a$ values of some selected compounds are listed in Table 1.7. Acids with $\text{p}K_a$ values lower than 1 are strong acid, those with $\text{p}K_a$ values between 1 and 3 are medium strength acids, and those with $\text{p}K_a$ values higher than 4 are weak acids. The $\text{p}K_a$ values of extremely weak acids are generally greater than 15.

Table 1.7 $\text{p}K_a$ values of some selected acids.

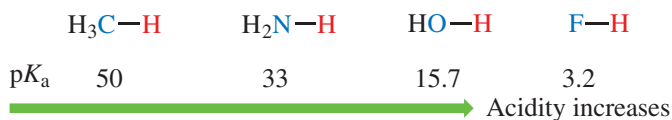
Acids	$\text{p}K_a$	Acids	$\text{p}K_a$
H_2SO_4	-10	HCN	9.1
HI	-9	NH_4^+	9.2
HBr	-8	Phenol	10.0
HCl	-7	CH_3OH	15.3
H_3PO_4	2.2	H_2O	15.7
HF	3.2	NH_3	33
HCOOH	3.75	H_2	38
CH_3COOH	4.76	CH_4	50
H_2S	7.0		

1.6.5.1 Factors Affecting the Acidity Strength of Organic Compounds

There are many factors that affect the acidity strength of organic compounds. The three most important factors are as follows:

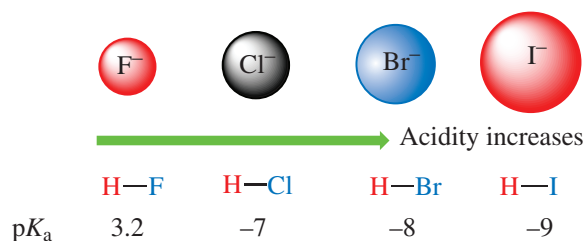
- Strength energy of the H-X bond
- Electronegativity of X
- Stability of X after dissociation

Because the effect of the H-X bond is weak compared with the other factors, we will focus on those other factors. When the $\text{p}K_a$ value of methanol (15.3) is compared with that of methane (50), the difference is very large. This difference can be explained by electronegativity. When we examine the $\text{p}K_a$ values of H-X compounds within a period in the periodic system, it is immediately recognized that the change is directly proportional to electronegativity. First, we will focus on individual atoms and we will use the simple organic compounds methane, ammonia, water, and hydrogen fluoride.

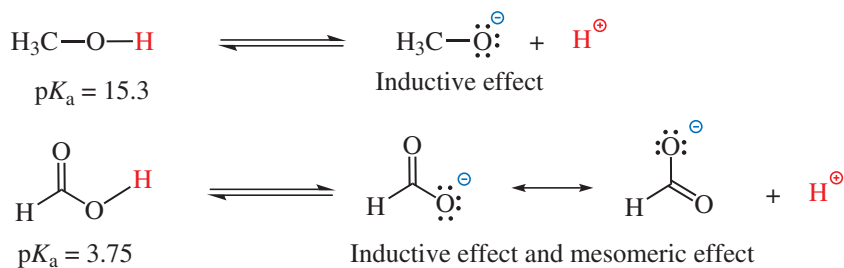


A clear trend can be seen by moving from left to right along the second row of the periodic table from carbon to fluorine. We have to consider the stability of the conjugate base in all cases. The negative charge ends up in each conjugate base. The electronegativity also increases by moving from left to right along a row of the periodic table. As the fluorine atom is the most electronegative of the four atoms and carbon the least, the strongest acid is HF. The bond electrons are withdrawn strongly and it becomes easier to separate the proton. The fluorine atom can stabilize the negative (-) charge better than the carbon atom.

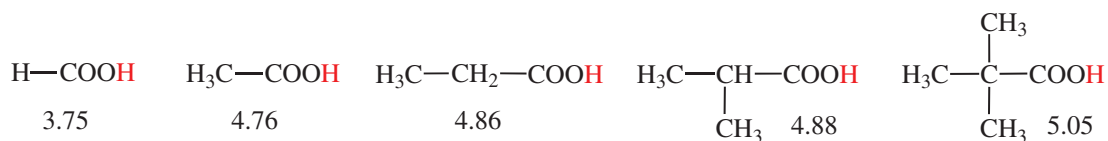
It turns out that when moving from top to bottom within a given column of the periodic table, we again observe a clear increasing trend in acidity. We cannot explain this trend by the electronegativity of the elements. Because the most electronegative element is fluorine, one would expect that HF would be the strongest acid. However, this is not the case; the strongest acid is HI. The stability of the conjugated base determines directly the strength of acids. As we go from top to bottom in a group, the radius of the elements increases because of the increasing number of shells. The atomic radius of iodine is approximately twice that of fluorine, and so in an iodide ion, the negative charge is spread out over a significantly larger volume. The larger the area where the charge is distributed, the more stable the ion is. As the iodide anion is more stable than the fluoride ion, HI can release the proton much more easily than HF.



After the proton has been removed from an acid molecule, the charge formed can be stabilized via both inductive and mesomeric effects. For example, let us examine the acid strengths in two different molecules, methanol and formic acid. In both cases, the removable proton is attached to an oxygen atom. Which O-H proton is more acidic, methanol or acetic acid? While the pK_a value of methanol is 15.3, the pK_a value of formic acid is 3.75. Deprotonation of methanol affords a methoxide ion, which has no resonance (only one Lewis structure can be drawn). The negative charge (–) on the oxygen atom is localized and can be only stabilized by the inductive effect of the oxygen atom. However, after the deprotonation of formic acid, the negative charge will be evenly distributed on both oxygen atoms through resonance. The negative charge will be stabilized by inductive as well as by mesomeric effects. Then, the acid strength increases by a substantial amount. As a result, formic acid is a much stronger acid than methanol. Furthermore, the formate ion is a weaker base than the ethoxide ion. Remember that weaker bases have stronger conjugate acids.



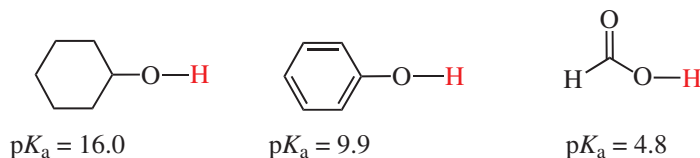
We have already discussed the influence of the inductive effect on the strength of acidity in the section. Here, we will give more examples. Because the carbon atom in a methyl group attracts bond electrons, the electron density around the carbon atom increases. Therefore, the methyl group donates bond electrons toward the adjacent carbon atom. Let us compare the acidity of formic acid with that of acetic acid. The pK_a value of formic acid is 3.75 while that of acetic acid is 4.76. The methyl group donates electrons toward the carbonyl group and this increases the electron density; as a consequence, the strength of acetic acid decreases. However, the argument here has nothing to do with resonance because no additional resonance contributors can be drawn for acetic acid. If one of the methyl protons in acetic acid is replaced with a methyl group (propionic acid), the strength of acidity is decreased from 4.76 to 4.86. However, this change is smaller than the change seen with formic acid because the number of bonds separating the methyl group and oxygen atom increases. Remember, the inductive effect decreases exponentially on a chain. As the number of methyl groups increases, the acid intensity decreases in parallel with the number of methyl groups.



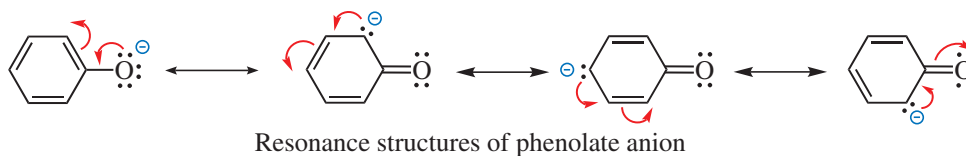
When the hydrogen atoms in the methyl group in acetic acid are replaced with halogens, the strength of the acids increases in parallel with the electronegativity of the halogen. The presence of chlorines clearly increases the acidity of the carboxylic acids. As chlorine is more electronegative than carbon, the chlorine withdraws the bonding electrons from the adjacent carbon atom toward itself and away from the carboxylate group. As a result, the electrons of the oxygen atom are drawn away from the O—H bond. Therefore, the proton can ionize easily. When more than one halogen atom is attached to the carbon atom, the strengths of acids increase according to the number of chlorine atoms (see also Table 1.3). Trichloroacetic acid falls into the strong acid class. Trifluoroacetic acid is stronger than trichloroacetic acid.



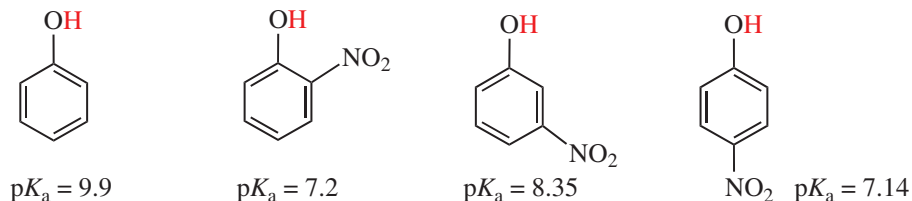
After examining how the inductive effect affects the $\text{p}K_{\text{a}}$ values of acids, let us now examine how the mesomeric effect changes their $\text{p}K_{\text{a}}$ values.



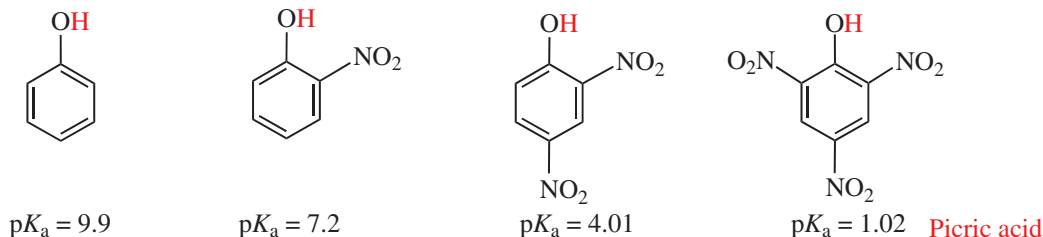
As is known, phenols are more acidic compounds than alcohols are. Phenol, for example, is about a million times stronger acid than cyclohexanol is but is weaker than organic acids. The alkoxide anion formed after the removal of a proton from cyclohexanol is stabilized only by oxygen's inductive effect because the conjugate base of cyclohexanol has a single resonance structure. However, the conjugate base of phenol is stabilized by distribution of the negative charge throughout the benzene ring by four significant resonance structures. This provides the stability of the phenolate, in other words, easier separation of the proton from oxygen.



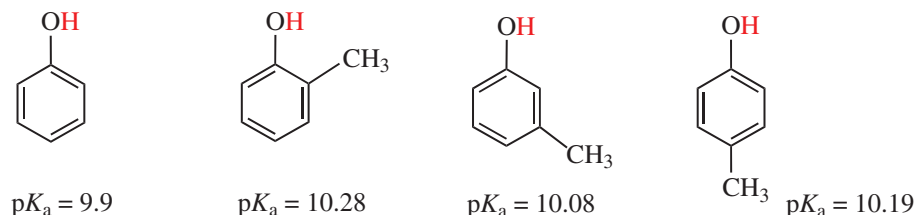
To increase the strength of acids, we have always emphasized that the remaining anion, formed after removal of the proton, should be stabilized as much as possible. This phenolic acidity can be further enhanced by attaching electron-withdrawing substituents to the ring. The positions of the groups are also very important. In the phenolate anion, the negative charge concentrates more on the *ortho* and *para* positions, and so it is more effective to connect the electron-withdrawing groups to these positions. It is noteworthy that the influence of a nitro group is over ten times stronger in the *para* position than it is in the *meta* position. *para*-Nitrophenol is more acidic than *ortho*-nitrophenol because of the strong intramolecular hydrogen bonding between the OH hydrogen and the NO_2 group.



Furthermore, additional nitro groups have an additive influence if they are positioned in *ortho* or *para* locations. The trinitro phenol is a very strong acid called picric acid.



Connecting electron-withdrawing substituents to the phenol ring increases acidity, while connecting electron-donating substituents reduces it. These groups increase the electron density on the ring, as well as on the phenol oxygen so that the proton cannot be easily released. Inductively, the electron-donating methyl group reduces the acidity of the phenol, albeit slightly, depending on its location.



1.6.6 pK_b Values of Bases

There is a close relationship between the acidity of acids and the basicity of bases. An easy way to look at basicity is based on electron pair availability. The more available the electrons, the more readily they can donate electrons to form a new bond to the proton, and therefore the stronger the base. The strength of a base is expressed by the pK_b value. In this section, we will focus on amine bases and show how base strengths are affected.

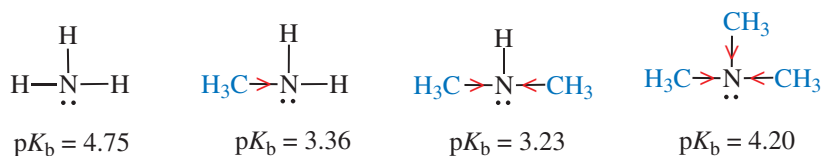
Weak bases do not have a large attraction for the proton of an acid. For example, ammonia is a weak base, and when it dissolves in water, a low concentration of ammonium hydroxide is formed. The position of equilibrium lies well to the left. When we take the H_2O concentration constant, the equilibrium is shown as follows. According to this equation, the smaller the pK_b value of a base, the stronger the base.



1.6.7 Factors Affecting the Strengths of Bases in Nitrogen-Containing Compounds

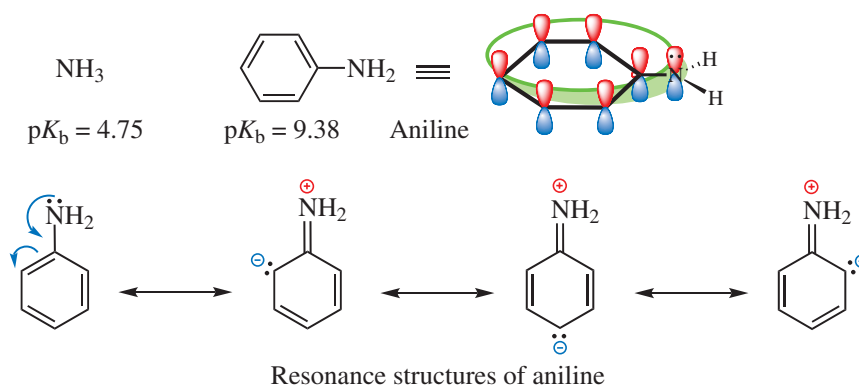
Neutral nitrogen compounds contain a pair of nonbonding electrons. Because this electron pair can bond the proton, nitrogen compounds fall into the base class. The groups that are attached to the nitrogen atom significantly affect the basicity depending on their electronic properties. Electron-donating groups have a tendency to push electrons toward the nitrogen atom and increase the electron density around the nitrogen atom, and this makes the lone pair even more attractive to hydrogen ions.

Ammonia has a pK_b value of 4.75. In general, primary alkyl amines are stronger bases than ammonia. A methyl group in methyamine decreases the pK_b value from 4.75 to 3.36 and a second methyl group to 3.23 as expected. Attachment of a third methyl group, contrary to expectations, increases the pK_b value. These values given below are observed in the aqueous environment.

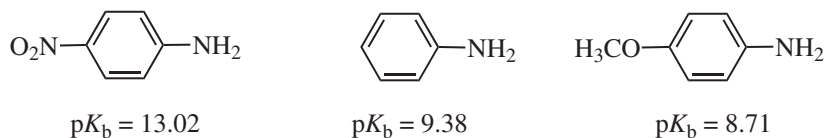


Two factors influence the strength of a base: how easily a lone pair picks up a proton and the stability of the ions being formed. The nitrogen atom turns into ammonium salt by abstracting a proton. We also need to discuss the stability of the ammonium ion formed by bonding a proton. In the aqueous environment, the ammonium ion can be stabilized by solvation of the water molecules. However, when three methyl groups are bonded to the nitrogen, the stability of ammonium salts decreases because of the hindered solvation. For this reason, the base strength decreases. Trimethylamine is only a slightly stronger base than ammonia despite the presence of three electron-donating alkyl groups. These three methyl groups take up quite a large space. As the nitrogen atom is crowded by the three alkyl groups, it makes it difficult for the nitrogen atom to approach another atom. To sum up, the inductive effect of the alkyl groups increases the base strength, while the reduced solvation and steric effects decrease it.

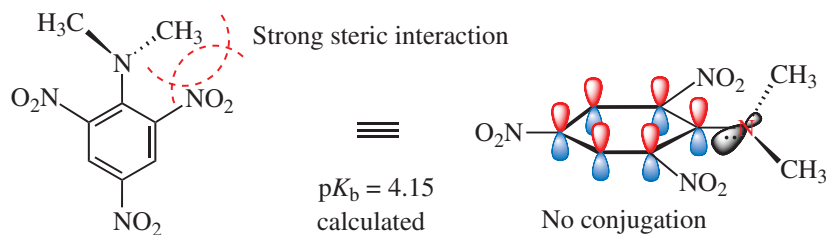
If one of the hydrogen atoms in ammonia is replaced by a benzene ring, the base strength of the compound (aniline) decreases. In order for a base to be strong, it is crucial that the nonbonding electrons be localized as much as possible. Aniline is a weak base because the lone pair on nitrogen is delocalized into the aromatic ring. This indicates that the nonbonding electrons are no longer fully available to bond a proton. In other words, electrons are delocalized, not localized. The electron density on the nitrogen atom decreases and it is not as much as that on the nitrogen atom in ammonia. Indeed, aniline is a weaker base than ammonia.



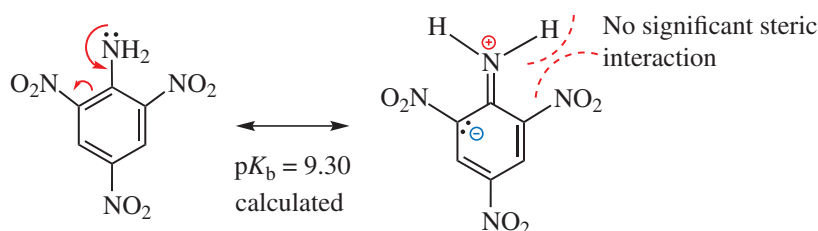
Substituted anilines of course have different basicities depending on the electronic nature of the substituent. For example, if an electron-withdrawing group such as a nitro group is attached to the *para* position (*p*-nitroaniline), the nonbonding electrons on the nitrogen atom will delocalize more in the ring and the base intensity will decrease because the nitro group will attract electrons more strongly. The measured pK_b value for nitroaniline (13.02) clearly indicates this finding. If the substituent attached to the ring is an electron-donating group because of the increased electron density on the ring, the delocalization of the free electrons on the nitrogen atom will be hindered. The stronger the electron donor on the ring, the higher the basicity of the aniline.



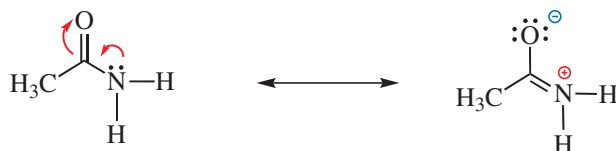
The effect of the substituents in the *ortho* position on the base strength can be either electronic or steric. Let us try to explain how the steric effect dominates over the electronic effect. When we compare the base strength of 2,4,6-trinitroaniline with that of *N,N*-dimethyl-2,4,6-trinitroaniline, the latter is known to be 40 000 times more basic. Of course, the methyl groups will increase the electron density on the nitrogen atom through their +I effects. However, this big difference cannot be solely attributed to the electron-donating effect of the methyl groups. This difference can only be explained by the steric effect. Of course, the three nitro groups will attract the nonbonding electrons on the nitrogen atom as we discussed in the case of aniline. When two methyl groups are attached to the nitrogen atom and if the base strength increases, the first thing that comes to mind is that the electrons cannot delocalize in the ring and they are localized on the nitrogen. *How can such a situation occur?*



The dimethylamino group is sufficiently large to interfere sterically with the very large nitro groups in both *o*-positions. Because of this steric interaction, a bond rotation about ring carbon to nitrogen occurs and the O atoms of NO_2 and the Me groups of NMe_2 move out of each other's way, so that the p orbital on the N atom is now no longer parallel to the p orbitals of the ring carbon atoms. As a consequence, the nonbonding electrons on the nitrogen cannot delocalize in the aromatic ring. For an ideal conjugation, parallel alignment of the orbitals is required. Localization of the bonding electrons on the nitrogen atom will increase the base strength. The presence of two hydrogen atoms on nitrogen does not lead to a steric interaction between the O atoms of NO and the protons of the NH_2 group.

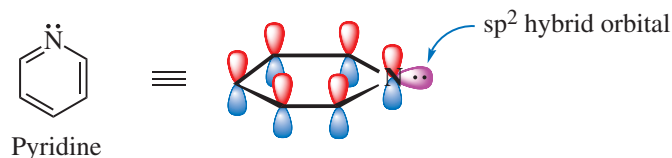


When the nonbonding electrons of a nitrogen atom conjugate with a carbonyl group, the base strength of the nitrogen atom is also reduced. For example, the nonbonding electrons on nitrogen in amides conjugate with the carbonyl group and the base strength decreases. Generally speaking, when a carbonyl group is attached to the nitrogen atom, the ability of the nitrogen atom to bond a proton decreases because of both the $-I$ and $-M$ effects of that group.

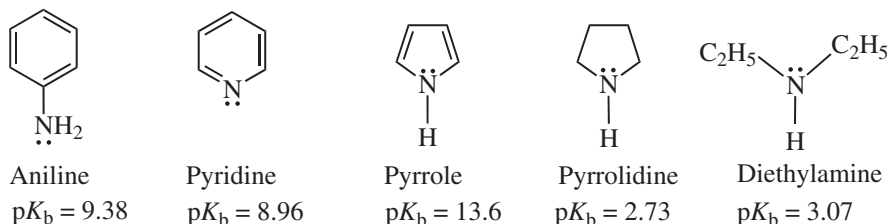


1.6.8 Heterocyclic Bases

Heterocyclic bases containing nitrogen atoms are the most commonly used bases in organic chemistry. Among these, pyridine has the widest area of use. The pK_b value of pyridine is 8.96. Pyridine is a weaker base than saturated amines. As can be seen from the drawing below, the sp^2 hybrid orbital bearing the nonbonding electrons is perpendicular to the p orbitals in the ring. They are not part of the aromatic sextet. In other words, the lone pair of electrons is not delocalized in the ring. Then, why is the base strength of pyridine weaker than that of aliphatic amines? We emphasized that the higher the s ratio in the hybridized orbitals, the more the electrons are attracted by the nucleus. In amines, hybridization of the nitrogen atom is sp^3 and the ratio of s is 25%. In pyridine, because of sp^2 hybridization, the ratio of s in hybrid orbitals is 33.3%. This indicates that the electrons in the sp^2 orbitals will be tightly bound by the nucleus. Therefore, the tendency of pyridine to bind a proton is weaker than that of aliphatic amines.



When pyridine and pyrrole are compared, it appears that pyrrole is a weaker base. In pyrrole, the nonbonding electrons of the nitrogen atom are involved in the conjugation with the two double-bond electrons of pyrrole to form a 6π electron system. Therefore, the nonbonding electrons in pyrrole are much less available for bonding to a proton. For these reasons, pyrrole nitrogen is not a base. Pyridine, on the other hand, already has a stable conjugated 6π electron system. Hence, the nonbonding electrons on the nitrogen atom in pyridine can be easily donated to a proton. On the other hand, pyrrolidine, a reduced form of pyrrole, is a strong base. There is no electron delocalization in this system; the electrons are localized on the nitrogen atom. The pK_b value of pyrrolidine is 2.73.



1.7 Reaction Kinetics and Energy Diagrams

Reaction kinetics is a field that investigates the rate of chemical reactions. *What is the mechanism of the reaction? What intermediates are occurring during a chemical reaction?* These questions should be addressed to understand how a reaction occurs. The energy change that occurs during the reaction is also very important in terms of the reaction mechanism. It is not sufficient to know the products formed to explain the mechanism of the occurrence of a chemical reaction. It is also necessary to know the intermediates formed between the reactant and the product. There are many experiments designed to investigate how reactions happen. One of these methods used is chemical kinetics, in which the rate of a reaction is measured. In most chemical reactions, compounds A and B do not directly form products. Intermediates often occur, and these intermediate products can form the product as well as return to the reactants.



What is the effect of energy on the chemical reaction? The effect of energy on reaction rates is indisputably important. Collision between the reactants is essential in order to react or change chemically. We should not expect all collisions between molecules to result in chemical reactions. For example, nitrogen and oxygen molecules are present in the air and they constantly collide. However, there is no chemical reaction between them as a result of these collisions. If collisions alone cannot explain reactivity, there must be other factors responsible for chemical reactions. The kinetic energy of molecules is important here. Slow moving molecules with lower kinetic energy do not take part in chemical reactions. Collisions between molecules with higher energy that lead to a chemical reaction are called *effective collisions*. We should then answer the question: *Why do reactions require collisions of molecules with high energy?* We know that during a chemical reaction, some bonds are broken and some bonds are newly formed. We know that breaking bonds requires energy and the formation of new bonds releases energy. The minimum energy required for an effective collision to break some bonds and start the reaction is called the *activation energy* (Figure 1.22).

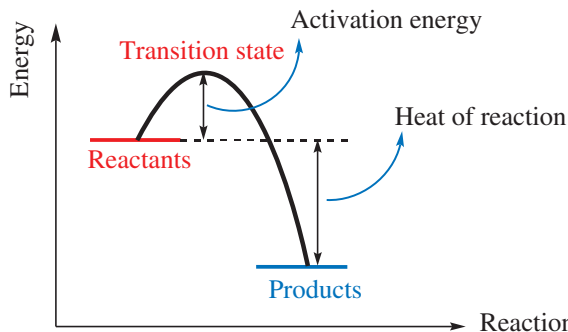
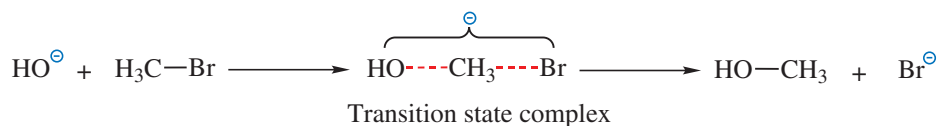


Figure 1.22 Reaction coordinates for an exothermic reaction and activation energy.

This diagram (Figure 1.22) plotting energy as a function of reaction progress is called a potential energy diagram. According to this diagram, reactants must reach a certain energy level. The energy rises to a maximum value called the *transition state*. At the transition state, the reactants have sufficient energy so that the bonds in the reactant start to break. The bonds to be broken in the transition complex are partially weakened and new bonds to be formed begin to form partially. Let us try to explain this phenomenon with a chemical reaction. In the transition state for the nucleophilic substitution reaction of methyl bromide by a hydroxide ion, a bond between the oxygen and carbon is partially formed and the bond between carbon and bromide is partially broken. The structure of the transition state lies somewhere between that of the product and that of the reactants. The dashed lines show partially broken and partially formed bonds.



The half-life of the transition state complex is very short. When moving to the right on the reaction coordinate, the system starts to release energy and begins to form products. The higher the activation energy, the slower the reaction; the lower the activation energy, the faster the reaction. For example, if the activation energy of a chemical reaction is 40 kcal/mol, the reaction rate will be indeterminably slow at room temperature (25 °C). This indicates that the reaction will not take place at room temperature. If the activation energy of a reaction is 15 kcal/mol, this reaction takes place quickly at room temperature.

To increase the rate of a reaction, the amount of energy required for the formation of the transition state must be reduced. Compounds that reduce the activation energy required for the formation of the transition state and increase the rate of a reaction are called *catalysts*. Catalysts are not consumed during the reaction, they actively participate in the formation of intermediates, and they do not appear in the net reaction equation. They are recovered after the reaction and certainly do not affect the energies of the reactants or products (Figure 1.23).

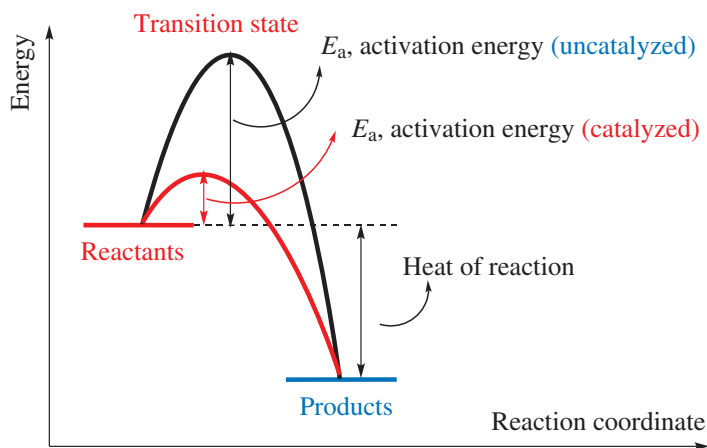
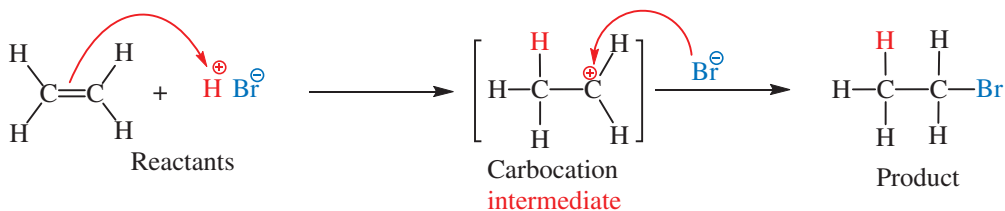


Figure 1.23 Potential energy diagram comparing catalyzed and uncatalyzed processes.

Chemical reactions cannot be limited to a single transition state. Some reactions occur in two or more steps as in the case of addition of HBr to ethylene. In the first transition state, double-bond electrons attack the proton of HBr and begin to bond it using the π electrons to the carbon atom. The energy then decreases until an *intermediate*, a carbocation, is formed. In the next step, which has its own activation energy, the carbocation starts to react with the bromide ion to form the final addition product (Figure 1.24).



The carbocation formed is more stable than either of the two transition states. In most cases, the intermediates are not stable and they cannot be isolated. One should not confuse intermediates with transition states. *Intermediates always have fully formed bonds, while transition states always have partially formed bonds.*

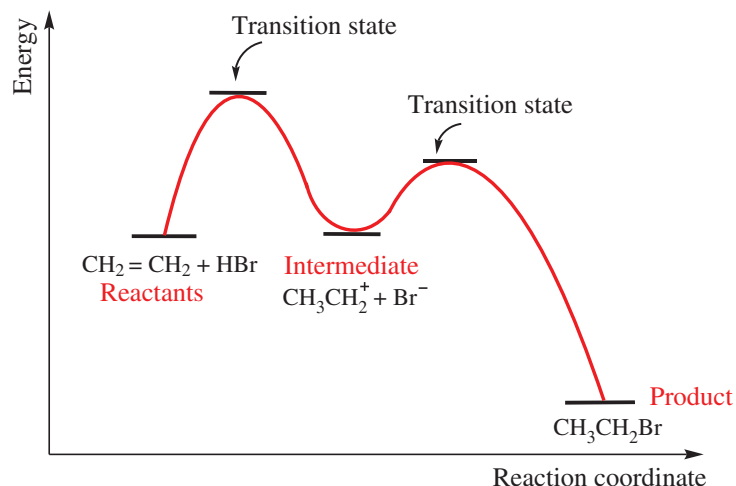
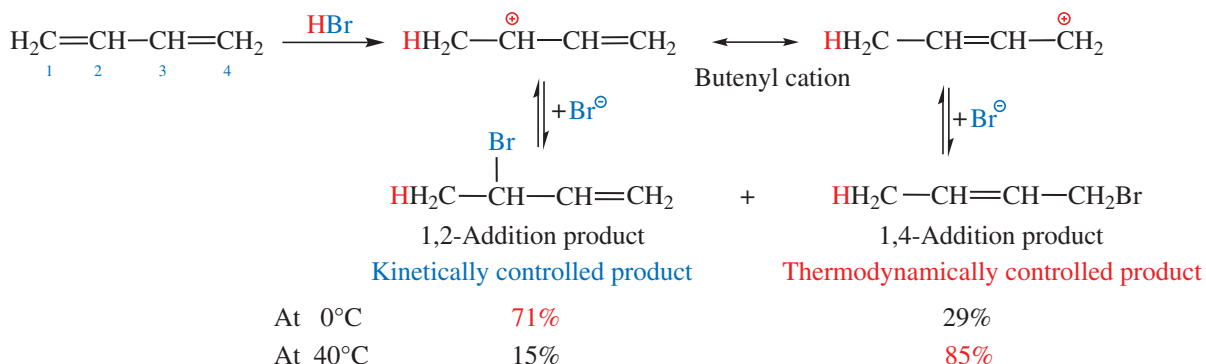


Figure 1.24 Reaction coordinate diagram for the addition HBr to ethylene.

1.7.1 Thermodynamic vs. Kinetic Control of Reactions

Let us discuss a chemical reaction in which two isomeric products are formed. The energies of these products will most likely be different. For example, conjugated dienes undergo electrophilic addition reactions to form a mixture of 1,2-adduct and 1,4-adduct. The reaction of hydrogen bromide with 1,3-butadiene gives different product distributions under different conditions. When the reaction is carried out at 0 °C, the major product is the 1,2-addition product. However, when the same reaction is carried out at 40 °C, the major product is the 1,4-addition product. When the structures of these molecules are compared, it is easy to recognize that the 1,4-addition product is more stable than the 1,2-addition product is. The 1,4-addition product is the thermodynamic product with the lowest energy. The 1,2-addition product is a less stable product called a kinetic product.



The first step is the protonation of one of the C=C double bonds in butadiene. The protonation occurs regioselectively and gives the more stable carbocation because of conjugation with the adjacent double bond. The positive charge (+) is distributed over two carbon atoms. The bromide ion can attack either carbon. Attacking the C2 carbon leads to the kinetic product; attacking the terminal carbon, C4, leads to the thermodynamic product. The activation energy leading to the 1,2-addition product is less than that leading to the 1,4-addition product, even though the 1,4-addition product is more stable. Therefore, at low temperature, 1,2-adduct, the kinetically controlled product, is formed as the major product. At low temperatures, formation of these products is irreversible. The energy is not enough to cross back over the barrier to form a butenyl cation. However, at higher temperatures, there is sufficient energy for both adducts to revert to the butenyl cation. Because the activation barrier for 1,2-adduct is smaller for conversion back to the butenyl cation than that for 1,4-adduct,

more 1,2-adduct will revert to the butenyl cation, which will again form both adducts. Finally, the equilibrium will shift to the side of the thermodynamically more stable product, the 1,4-addition product. In summary, the 1,2-adduct is the *kinetically controlled product* with the lower activation barrier, while the 1,4-adduct is the *thermodynamically controlled product* with the higher activation barrier (Figure 1.25).

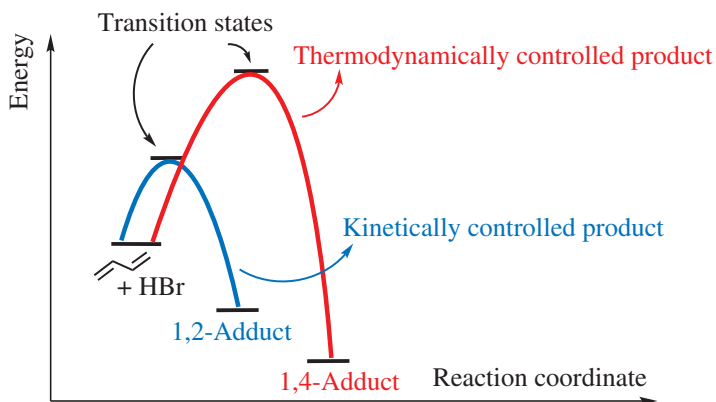
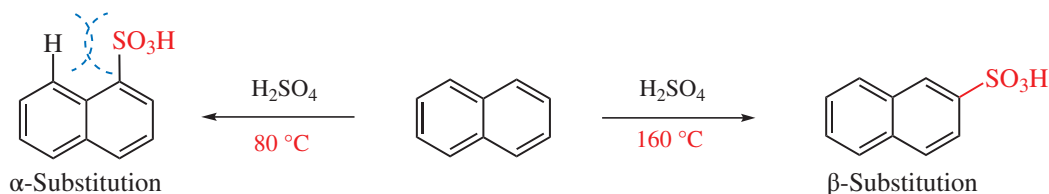


Figure 1.25 An energy diagram for the formation of 1,2-adduct and 1,4-adduct.

In contrast to many other electrophilic aromatic substitution reactions, aromatic sulfonation is reversible; in other words, it is an equilibrium. Two products are formed in the sulfonation reaction of naphthalene. The α -substitution product is less stable and occurs at 80 °C. The β -substitution product is thermodynamically more stable and occurs at 160 °C. Therefore, the transition state leading to the α -substitution product will be lower in energy and it will be formed fastest. Therefore, the α -substitution product is the kinetically favored product. However, the β -substitution product is more stable than its α -isomer is. This is due to the 1,8 steric repulsion present in the α -isomer. Again, here is also an equilibrium between naphthalene and the products. The formation of such a balance at high temperature is demonstrated by the conversion of the α -substitution product into a β -substitution product when heated to 160 °C.



1.7.2 Reaction rate

Knowing whether a chemical reaction is endothermic or exothermic does not give us any information about the reaction rate. The activation barrier must be overcome first. Otherwise, a chemical reaction cannot proceed. Therefore, there are several factors that affect the reaction rate. What are these factors?

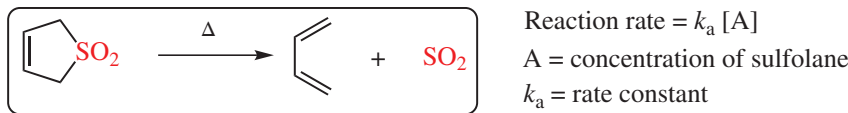
- Number of collisions between molecules in a given unit of time and volume,
- Number of colliding molecules with sufficient energy,
- Number of molecules colliding in the appropriate position.

These three factors determine the speed of chemical reactions. The first is called the collision frequency, the second the energy factor, and the third the orientation factor. The reaction rate directly depends on the concentration of the reactants. The higher the reactant concentration, the greater the probability of molecules colliding. The speed of each reaction is different and the reaction rate is determined by experiments.

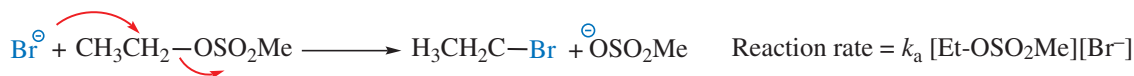
A chemical reaction takes place when particles collide in the correct orientation and with sufficient energy. If they do not collide, there can be no reaction. These parameters can either speed up or slow down the rate of the reaction.

Some reactions contain only one reactant. For example, when sulfolane is heated, SO₂ is released and it turns into butadiene. Because there is only one reactant in this reaction, the reaction rate directly depends on the concentration of sulfolane.

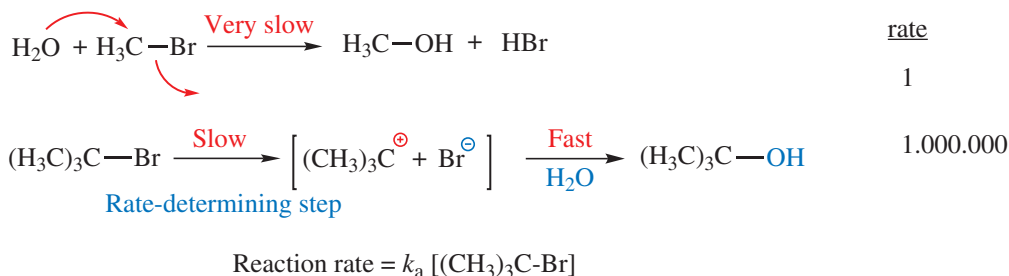
If its concentration is doubled, the reaction rate is doubled. The reaction rate formula is given below. The rate is directly proportional to the concentration of the reactant. Such reactions are called *first-order reactions*.



Let us look at the kinetics of a simple nucleophilic substitution reaction, the reaction of ethyl mesylate with Br^- . If we double the concentration of mesylate, we find that the rate of the reaction also doubles. Similarly, if we double the concentration of the Br^- ion, the reaction rate will again double. In this case, the rate of the reaction linearly depends on the concentration of two species. This reaction is called a *second-order reaction*.



Most nucleophilic substitution reactions take place by this mechanism discussed above. However, when a substitution reaction is carried out with an unhindered substrate, such as methyl bromide with a neutral nucleophile (H_2O) in a protic solvent, the reaction is one of the slowest substitution reactions. When the same reaction is carried out with *t*-butyl bromide and water, the reaction is one million times faster to give *t*-butanol. The rate of this reaction depends only on the concentration of *t*-butyl bromide. The mechanism of this reaction differs from the mechanism shown above. In the first step, the leaving group (Br^-) leaves and then a carbocation is formed. This step is the rate-determining step. The formation of a bond between the nucleophile and the carbocation in the second step occurs rapidly. In the rate-determining step, only one substrate is involved. Therefore, the rate of the reaction depends only on the concentration of *t*-butyl bromide. Hydrolysis of CH_3Br is a second-order reaction. The rate of the reaction depends on the concentration of CH_3Br and H_2O . However, if water is used as a solvent (large excess), only a small fraction of water in excess will be consumed, and its concentration can be considered to stay constant. The rate of the reaction will depend only on the concentration of CH_3Br . This is also a *first-order reaction*, although two different substrates are used as the starting materials.



A molecule can undergo a reaction with itself. Such reactions are also second-order reactions. In such a reaction, if the concentration of molecule A is doubled, the reaction rate is quadrupled.

$$\text{Reaction rate} = k_a [A] [A] = k_a [A]^2$$

The reaction rate should not be confused with the rate constant. The reaction rate depends on concentration and the rate constant. However, the rate constant k_a is not a concentration-dependent parameter. The value of the rate constant depends on the temperature and the activation energy E_a and is expressed by the Arrhenius equation.

$$\text{Arrhenius equation } k = Ae^{-\frac{E_a}{RT}}$$

k = rate constant

E_a = activation energy

T = temperature (K)

A = a constant for the frequency of particle collisions (frequency factor).

Here, E_a is the activation energy. As E_a increases, k will be smaller, and a smaller rate constant corresponds to a slower chemical reaction. Temperature appears in the exponent and therefore the rate constant will be very sensitive to this parameter. Small changes in temperature can have a drastic effect on the rate of the reaction. Frequency factor A is a measure of the number of molecules colliding at the appropriate position. It varies slightly with temperature. During the reaction,

only a small part of the colliding molecules collide into the product (in the appropriate position), and the energy of a small proportion of the colliding molecules is sufficient to form the product.

The Arrhenius equation indicates that the reaction rate depends on the number of molecules with kinetic energy of at least E_a . Not all molecules at a given temperature have the same kinetic energy. The energies and numbers of molecules in a gas phase are shown in the graphic in Figure 1.26. The red curve shows the energy distribution of molecules at room temperature, while the blue curve shows the energy distribution of molecules at a higher temperature. Suppose the activation energy required for a reaction is 20 kcal/mol. The activation energy is shown with a dashed black line. The shaded area on the right side of the line where this line crosses the red curve shows the amount (fraction) of molecules that have the activation energy necessary for the reaction to occur. If the activation energy is 40 kcal/mol, the number of molecules with this energy appears to be very low. When the reaction temperature is increased (blue curve), the number of molecules with the activation energy required for the reaction increases (the entire shaded area). This indicates that the reaction rate increases with increasing temperature.

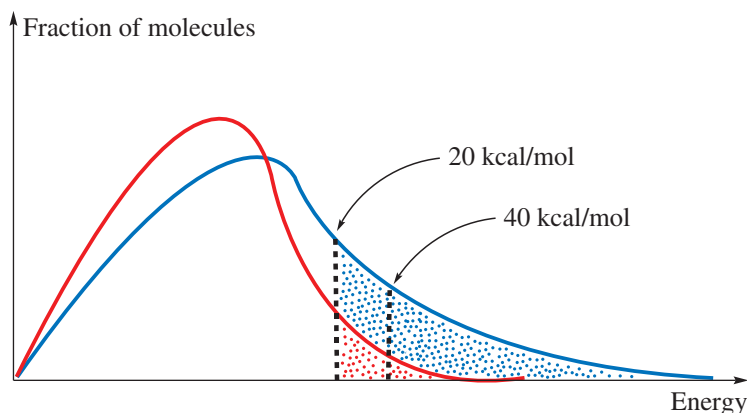
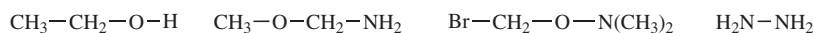


Figure 1.26 Variation in the kinetic energy of the molecules with temperature. Red curve: room temperature, blue curve: a higher temperature.

Problems

1.1 What is the hybridization of each bond (10 bonds) in propane ($\text{CH}_3\text{CH}_2\text{CH}_3$).

1.2 Find out from which orbitals the bonds are formed in the following molecules.



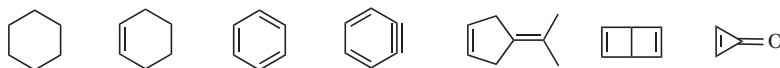
1.3 Determine the hybridization of all the bonds of the following compounds.



1.4 Determine the hybridization of the carbon atoms in the following compounds. Draw the molecules with their orbitals and discuss the positions of the hydrogen atoms.



1.5 Determine the hybridization of the carbon atoms in the molecules whose structures are given.



1.6 Determine the hybridization of the carbon atoms of the following molecules.



- 1.7 In the molecule below, determine the five-membered rings' position relative to each other, taking into account the hybridization.

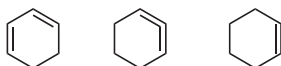


- 1.8 Discuss the conformation of butadiene, taking into account the hybridization of butadiene carbon atoms.

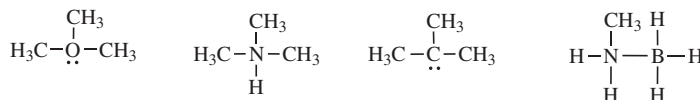
- 1.9 Discuss the geometric structures of the molecules below, taking hybridization into account.



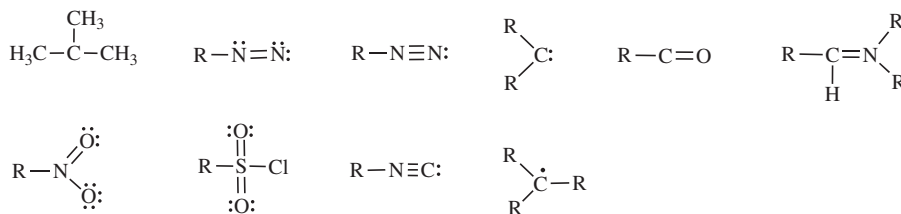
- 1.10 Discuss the stability of the molecules below, taking hybridization into account.



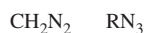
- 1.11 Find the formal charges of the following compounds.



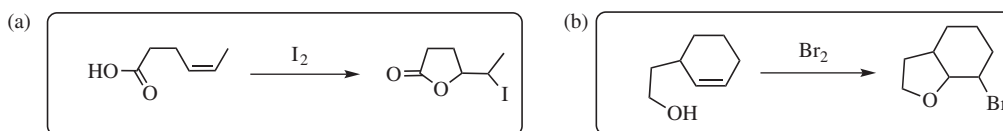
- 1.12 Find the formal charges of the elements given below.



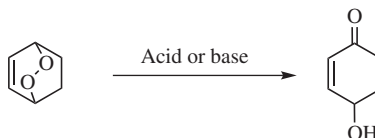
- 1.13 Write the resonance structures of the following compounds and the formal charges of the atoms involved.



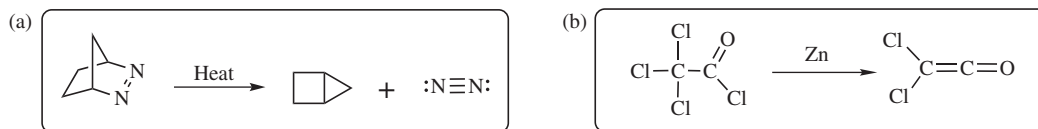
- 1.14 Find the oxidation numbers of the central atoms reacting in the reactions given below and discuss the reactions in terms of oxidation and reduction.



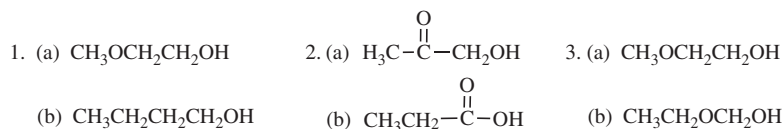
- 1.15 Unsaturated bicyclic endoperoxides rearrange into unsaturated hydroxy ketones in the presence of a base or an acid. Discuss this transformation in terms of oxidation and reduction.



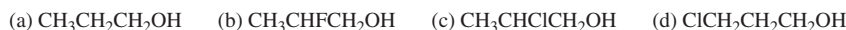
1.16 Let us examine the reactions given below in terms of oxidation and reduction.



1.17 Which of the following compounds is the stronger acid?



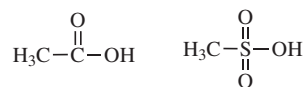
1.18 Sort the following molecules according to their acidity strength.



1.19 Sort the following molecules according to their acidity strength.

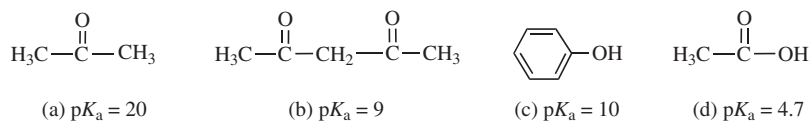


1.20 Which of the following compounds is more acidic?



1.21 HCl is a weaker acid than HBr. ClCH_2COOH is a stronger acid than BrCH_2COOH . Give a reasonable explanation.

1.22 Sort the following molecules according to their acidity strength.



1.23 Which of the above compounds reacts with NaOH? ($\text{p}K_a$ value of $\text{H}_2\text{O} = 15.7$).

1.24 Does the *t*-butoxide anion ($\text{KOC}(\text{CH}_3)_3$) react with H_2O ? Can an aqueous solution of this anion be obtained?

1.25 We have two bottles. In one bottle, we have phenol ($\text{p}K_a = 9$) and in the other we have an organic acid, which is not soluble in water ($\text{p}K_a = 5.0$). How can we distinguish between the two compounds using sodium bicarbonate (NaHCO_3) ($\text{p}K_a$ value of $\text{H}_2\text{CO}_3 = 6.4$)?

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