The Chemistry of Biomolecules

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By

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PREFACE

In the past, it was believed that organic compounds could only be produced by living organisms but could not be made by humans. However, along with the development of synthetic chemistry, organic chemistry is no longer related to only living organisms. Biomolecules are special organic compounds, a group of substances produced and metabolised by living organisms in order to sustain life. Life phenomena are not special incomprehensible magical phenomena but are the result of the structure of biomolecules and the functions produced from them. Molecules are physically stable groups of atoms and have structures and properties that depend on the properties of the atoms involved. In living organisms, in particular, biomolecules cooperate to form a self-regulatory mechanism, in other words, a cleverly programmed mechanism, to sustain life through a variety of functions of the molecules. Recently in life sciences, we have tried to understand the mechanisms of life phenomena in chemical terms, that is, at the level of organic molecules. In order to study such life phenomena, we must first deepen our understanding of the structure and the physical and chemical properties of organic compound molecules. Thus, the divide between organic chemistry and biosciences has recently been lowered again. Based on the orbital theory developed from quantum mechanics, this book begins with an explanation of the mechanisms of the formation of chemical bonds to understand the building of various molecules precisely and then explores why stable and unstable molecules are formed. Their structures cause unique, organic chemical reactions. Based on fundamental theories such as the molecular orbital method, thermodynamic law, frontier orbital theory, and molecular interactions, which have not been covered in basic organic chemistry textbooks, we will advance our understanding of the functions of biomolecules. In the second half, carbohydrates, lipids, proteins, and nucleic acids are used as examples of basic and important biomolecules, and an understanding of their structures and reactions will be established. Based on the basics of organic chemistry learned in this book, I would like you to proceed to the next stage of learning biochemistry.

I am thankful to Professor Dr Naruyoshi Komiya at the Jikei University School of Medicine for his cooperation and to Professors Dr Tadashi Sasaki, Dr Shoji Eguchi, Dr Katsumaro Minamoto, and Dr Masatomi Ohno at Nagoya University for their long-time guidance. In addition, I am grateful to Mrs Elanor Harris for her professional proofreading.

Takashi Okano, Tokyo, 2023
Professor Emeritus of Chemistry, the Jikei University, School of Medicine, Tokyo, Japan

Chapter 1 Constitution of Atoms and Molecules

1-1 Constitution of atoms and atomic orbitals

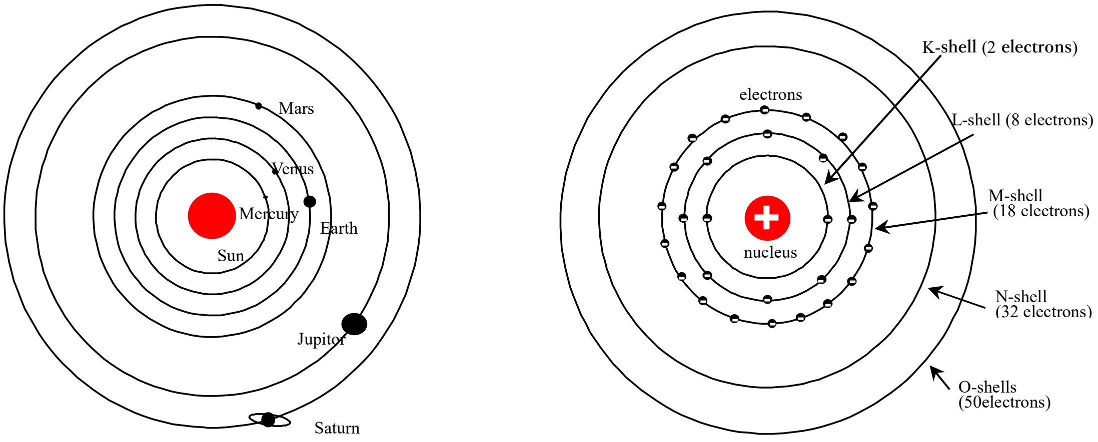
Living organisms are composed of organic molecules; substances centred on carbon. Organic chemistry was originally a chemistry that dealt with substances of biological origin, but now it deals with both biological and artificial. It is a chemistry that investigates the properties and changes of carbon substances. What is the principle of the constitution of everything, including biomolecules and inanimate objects?

When a liquid or solid substance is cut into small pieces so that its properties do not change, the smallest structure is a molecule, the unit of substances. If the molecule can be broken down further, it will reach a constituent unit called an atom. Looking closely, it can be seen that the more detailed structure of atoms is divided into atomic nuclei and electrons. Dividing it more finely, the nucleus can be divided into protons, neutrons, and even smaller elementary particles, but they are not what chemistry deals with. The proton in the nucleus has a positive charge, and the electron has a negative charge. Therefore, the Coulomb attraction between the nucleus and the electron exists, and the nucleus is almost fixed due to the difference in mass, and the electrons are moving around the nucleus by the coulombic force. We can think of a classical atomic model in which an electron moves around the nucleus under coulombic force, which decreases inversely proportional to the square of the distance between the nucleus and the electron (Fig. 1-1). We often see a figure in which an electron moves around an atomic nucleus. At first glance, it resembles the solar system's structure that is orbiting with a universal gravitational force that is also inversely proportional to the square of the distance between the sun and the planet. The mass and initial velocity of the planets determine the paths. While each planet moves almost independently, the orbits of the electrons are fixed, and each orbit is said to have multiple electrons. Where does this difference come from?

Quantum mechanic research has been active since the beginning of the 20th century when Albert Einstein discovered the particle (material) properties of light (waves). This revealed that particles also have wave properties, shown by Louis V. de Broglie as the wavelength of the material wave as de Brogile's equation (1-1)

$$\lambda = \frac{h}{mv} \tag{1-1}$$

where m is particle mass, v is particle velocity, h is Plank constant and λ is the wavelength of the material wave. This relationship was extended by Erwin A. R. J. Schrödinger and established as a



Solar system model

Atomic model

Fig. 1-1. Models of the solar system and atoms: Planets and electrons are orbiting with an attractive force that is inversely proportional to the square of the distance from the sun and atomic nucleus that exist in the centre. However, in the solar system model, each planet moves independently, whereas in the atomic model, multiple electrons are in the same orbit, or electrons can exist only in a fixed place.

quantum mechanical wave equation (**Schrödinger equation**) showing the energy conservation law in combination with the classical wave equation that expresses the spatial propagation of waves (1-2) as

$$-\frac{\hbar^2}{2m}\left(\frac{\partial^2\psi}{\partial x^2}+\frac{\partial^2\psi}{\partial y^2}+\frac{\partial^2\psi}{\partial z^2}\right)+V(x,y,z)\psi = E\psi \tag{1-2}$$

where, $\hbar = \frac{h}{2\pi}$, $V(x, y, z)$ is the mechanical potential energy, and E is the total energy of the particle. If $\psi(x, y, z)$ called **wave function** appearing in this equation is summarised on the left side, it can be written in the form of equation (1-3) as

$$H\psi = E\psi \tag{1-3}$$

where H is called the Hamiltonian operator. Applying the Hamiltonian operator to the wave function can derive the particle's total energy. It is difficult to think about the meaning of this wave function $\psi(x, y, z)$, but after that, the square of the wave function ($\psi(x, y, z)^2$) has come to be interpreted as representing the probability of a particle moving under the mechanical potential energy $V(x, y, z)$ in a micro space $dxdydz$.

In the wave equation of a particle of mass m moving freely in a one-dimensional box of length L, under no mechanical potential ($V = 0$), it never leaves the box, and there are no particles and $\psi(0) = 0$ and $\psi(L) = 0$ at the boundary of the box ($x = 0$ and $x = L$). When the wave equation is solved under such boundary conditions, the function that second order differential returns to the original function is a trigonometric function, and the solution like equations (1-4) (1-5) is obtained as

$$E_n = \frac{n^2 h^2}{8mL^2} \qquad (1\text{-}4)$$

$$\psi_n = \sqrt{\frac{2}{L}} \sin\left(\frac{n\pi x}{L}\right) \quad n = 1, 2, 3.... \qquad (1\text{-}5)$$

where number n is called a **quantum number** and must be an integer to satisfy the boundary conditions. Therefore, the wave function's energies of E_1, E_2, E_3 ... increase as the quantum number increases. These take discontinuous values stepwise, and the stepwise energy values of wave functions are called energy levels. Such discontinuity of physical quantities is called quantisation. Also, as n increases, the wavelength of ψ_n ($\lambda = 2L / n$) becomes shorter, and the number of points where $\psi_n = 0$ increases. The place where $\psi_n = 0$ is called a **node**, and the wave function with many nodes has a higher energy level.

In the motion of electrons attracted to the nucleus, the coulombic force, which is inversely proportional to the square of the distance to the nucleus, is the mechanical potential. This second-order partial differential equation gives a mathematically exact solution for one electron (charge: $-e$), such as a hydrogen atom and one nucleus (nuclear charge: $+Ze$). When a three-dimensional wave equation is solved using polar coordinates, the wave function of the solution is the product of a function that depends on the radial diameter r from the nucleus $R_{n,l}$ (radial distribution function) and a function $Y_{l,m}$ (spherical harmonics function) that depends on the angular direction (1-6) as

$$\psi_{n,l,m} = R_{n,l} \times Y_{l,m} \qquad (1\text{-}6)$$

where $n = 1, 2, 3, 4...$ $l = 0, 1, 2, ..., n - 1$ $m = -l, -l + 1, ..., 0, ..., l - 1, l$. In detail, these functions of $n = 1, 2, 3$ are as follows where μ is reduced mass, Z is the nuclear charge, ε_0 is vacuum dielectric constant, e is the electronic charge, $r = (x^2 + y^2 + z^2)^{½}$, and a_0 is Bohr diameter.

Radial distribution functions $R_{n,l}$:

$$a_0 = \frac{\varepsilon_0 h^2}{\pi \mu e^2} \qquad R_{1,0} = 2\left(\frac{Z}{a_0}\right)^{\frac{3}{2}} \mathrm{e}^{-\frac{Zr}{a_0}} \qquad R_{2,0} = \frac{1}{2\sqrt{2}}\left(\frac{Z}{a_0}\right)^{\frac{3}{2}}\left(2 - \frac{Zr}{a_0}\right)\mathrm{e}^{-\frac{Zr}{2a_0}} \qquad R_{2,1} = \frac{1}{2\sqrt{6}}\left(\frac{Z}{a_0}\right)^{\frac{3}{2}} \frac{Zr}{a_0}\mathrm{e}^{-\frac{Zr}{2a_0}}$$

$$R_{3,0} = \frac{2}{81\sqrt{3}}\left(\frac{Z}{a_0}\right)^{\frac{3}{2}}\left\{27 - 18\left(\frac{Zr}{a_0}\right) + 2\left(\frac{Zr}{a_0}\right)^2\right\}e^{-\frac{Zr}{3a_0}} \qquad R_{3,1} = \frac{4}{81\sqrt{6}}\left(\frac{Z}{a_0}\right)^{\frac{3}{2}}\left\{6\left(\frac{Zr}{a_o}\right) - \left(\frac{Zr}{a_0}\right)^2\right\}e^{-\frac{Zr}{3a_0}}$$

$$R_{3,2} = \frac{4}{81\sqrt{30}}\left(\frac{Z}{a_0}\right)^{\frac{3}{2}}\left(\frac{Zr}{a_0}\right)^2 e^{-\frac{Zr}{3a_0}}$$

Spherical harmonics functions $Y_{l,m}$:

$$Y_{0,0} = \frac{1}{\sqrt{4\pi}}$$

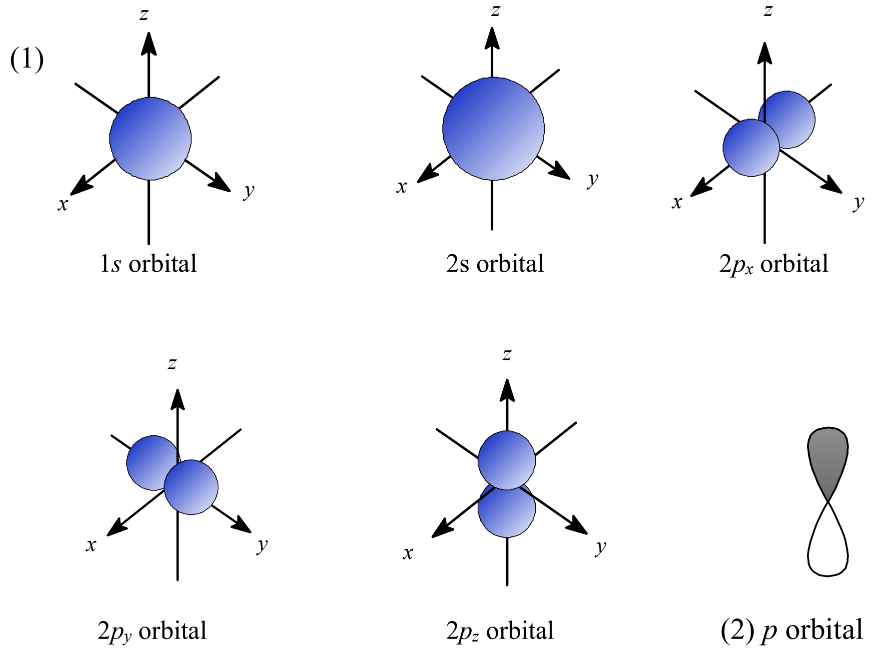
$$Y_{1,-1} = \sqrt{\frac{3}{4\pi}}\frac{y}{r} \qquad Y_{1,0} = \sqrt{\frac{3}{4\pi}}\frac{z}{r} \qquad Y_{1,+1} = \sqrt{\frac{3}{4\pi}}\frac{x}{r}$$

$$Y_{2,-2} = \sqrt{\frac{15}{4\pi}}\frac{xy}{r^2} \quad Y_{2,-1} = \sqrt{\frac{15}{4\pi}}\frac{yz}{r^2} \quad Y_{2,0} = \sqrt{\frac{15}{16\pi}}\frac{1}{r^2}\left(3z^2 - r^2\right) \quad Y_{2,+1} = \sqrt{\frac{15}{4\pi}}\frac{zx}{r^2} \quad Y_{2,+2} = \sqrt{\frac{15}{16\pi}}\frac{1}{r^2}\left(x^2 - y^2\right)$$

In these functions, three types of quantum numbers, n, l, and m, appear in the wave function. The number n is called the **main quantum number**, which is related to the radius of the nucleus and the electron and determines the electron's energy. The numbers that n can take are the integers 1, 2, and 3. The energy of an electron in a hydrogen-type atom is quantised to discontinuous values. The energy value of each wave function corresponding to n is the energy level. The two other quantum numbers, l and m, are quantum numbers that depend on the angular part of the wave function and are called **azimuthal quantum number**s and **magnetic quantum number**s, respectively, and are related to the angular momentum of an electron. These depend on the main quantum number n, where l is an integer from 0 to $n - 1$, and m is an integer from $-l$ to $+l$. The different set of the three quantum numbers determines the electron's motion of different energy in an atom.

Since it is interpreted that the square of the wave function $\psi(x, y, z)^2$ represents the probability of the existence of an electron at the coordinates (x, y, z), the graph obtained by plotting this function value in a three-dimensional space is the shape of the space in which the electrons are moving. This area of electron existence, which is the wave function, is called an **orbital** in relation to the orbit of the motion of planets in the solar system. Thus, the wave function is orbital. Because it is an orbital function of an atom, it is called an **atomic orbital** (**AO**). The square of an atomic orbital indicates the probability of the existence of an electron at that coordinate. If so, it is the **electron density**. Since the total probability of finding the one electron in question in the entire space is 1, the integral of the square of an atomic orbital function in the entire space should be 1 (normalised), and the integral of the product of two different atomic orbital functions in the entire space should be 0 (orthogonal). When $l = 0$, it is spherically symmetric, and there is no bias to the orbital function in any direction. However, when $l = 1$, it can be seen that the electron density depends on the value of m, and the function value differs depending on the direction. Because, in this anisotropic way, the difference in l greatly changes the direction in which electrons exist, the atomic orbital function corresponding to the value of l is named. In combination with the properties obtained from atomic spectroscopy, they are ***s* orbital** ($l = 0$), ***p* orbital** ($l = 1$), ***d* orbital** ($l = 2$), and ***f* orbital** ($l = 3$). In combination with the main quantum number n, they are called 1*s* orbital, 2*s* orbital, 2*p* orbital, 3*s* orbital, 3*p* orbital, and *3d* orbital, respectively. There are three types of *p* orbitals with different *m*, and they are named p_y orbital

($m = -1$), p_z orbital ($m = 0$), and p_x orbital ($m = +1$), respectively, from the direction in which the orbitals are distributed. Fig. 1-2 shows a picture of a region with a large electron density, the region with a large orbital function value, for the atomic orbital functions of the *s* orbital and the *p* orbital. The *s* orbital has no directionality and has a spherical spread, and the function value is positive over all regions, but it has a hollow shape and a node in which no electron exists near the central nucleus. The *p* orbital has two regions with high electron density, which is called the **lobe**, in each coordinate axis direction, and the value of the orbital function has a different sign across the node of the coordinate direction, as can be seen from the function formula of Y_1, and each has a different sign. If the coordinates are positive, the function value is positive; if the coordinates are negative, the function value is negative. The change of sign of the wave function value is called the **phase**, which is important when a bond is formed.



1*s* orbital

2s orbital

$2p_x$ orbital

$2p_y$ orbital

$2p_z$ orbital

(2) *p* orbital

Fig. 1-2. Forms of hydrogen atom type wave functions: (1) The function values of $2p_x$, $2p_y$, and $2p_z$ orbitals have different signs in the direction of the axis. The *p* orbital is often drawn in the shape shown in (2), paying attention to the phase and the orbital function value.

The wave equation could be solved mathematically in the case of hydrogen-type atoms. However, in multi-electron atoms after helium, there is a repulsive force between electrons, and the distance is not always constant because the electrons are moving. In such a case, the wave equation cannot be solved mathematically. Therefore, it will be corrected later after using the orbital function obtained by the hydrogen-type atom.

In the state where the atom has the lowest energy and is stable (the ground state), can all the electrons be in the 1*s* orbital? Although the position of an electron cannot be specified due to the nature of the wave function, two electrons cannot occupy one place at the same time due to the physical premise. The simultaneous existence of two electrons in the 1*s* orbit violates this principle and is not allowed. From this principle, called **Pauli's exclusion principle**, it is expected that the first electron occupies the 1*s* orbital, and the following electrons are buried sequentially from the orbitals with lower energy levels, such as 2*s*, 2*p*, and 3*s*. However, when the electrons are filled in this order, the problem is that they do not satisfy the already known chemical law (the **periodic table**) that was known before quantum mechanics was born. It has already been shown by the magnetic research of electrons that there are two types of electrons. Assuming a rigid sphere with negatively charged electrons, an induced magnetic field, called the spin, will be generated during rotation. When electrons are placed in a fixed magnetic field, two types of precessional motion of the magnetic dipole are observed due to the influence of the induced magnetic field. From the model shown in Fig. 1-3, there are two types of induced magnetic fields of electrons in the direction of this fixed magnetic field. These two magnetic properties were associated with the **spin quantum number** m_s, and the spin of the same direction for the external fixed magnetic field vector is α spin ($m_s = +1/2$), while the antiparallel spin is β spin ($m_s = -1/2$).

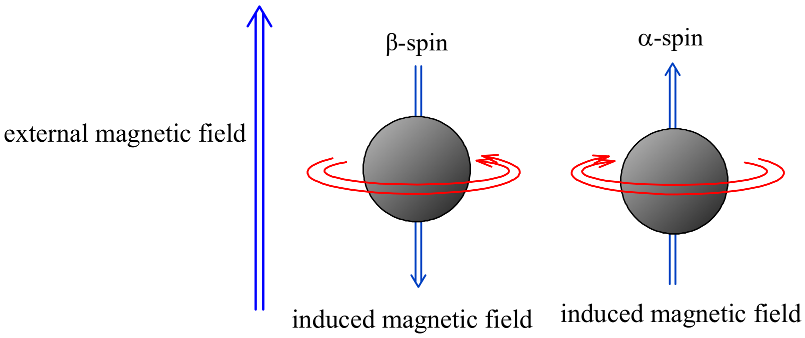


Fig. 1-3. Electronic spin: When a rotating electron is placed in a magnetic field, it is divided into energetically stable α-spin ($m_s = +1/2$) and unstable β-spin ($m_s = -1/2$). However, since the electrons do not distinguish between the north pole and the south pole, the direction of rotation cannot be distinguished. It should be considered as a purely quantum mechanical property. The direction of the spin and the direction of the external magnetic field are not parallel or antiparallel, but precession of spins with an angle is observed. The axis of rotation of precession is parallel or antiparallel to the external magnetic field.

In the figure, α-spin is represented by an up arrow, and a down arrow represents the β-spin. Both αβ spins have the same energy without an external magnetic field, but when placed in a fixed magnetic field, an energy difference proportional to the magnetic field strength appears, resulting in α spins at the low energy level and β spins at the high energy level. Since the electrons of both αβ spins have different properties, they can coexist in one orbital. Adding the spin quantum number rewrites Pauli's exclusion principle as "only two electrons with different spins can exist in one orbital". As a result, two electrons fit in the 1*s* orbital, and then two electrons fit in each orbital of 2*s*, 2*p*, and so on to form an atom. An occupied orbital is called an orbital in which two electrons fit and satisfy the Pauli exclusion principle. As the main quantum number n increases, the electrons move away from the nucleus, the energy of the electrons increases as the number of electrons existing in the orbital increases, and as n increases by 1, the number of electrons increases, and electrons form like a shell. The group of electrons corresponding to the main quantum number is called the electronic shell, and each shell is named K shell ($n = 1$), L shell ($n = 2$), M shell ($n = 3$), and N shell ($n = 4$), respectively. The electron shell is also called the major shell, and the orbitals, due to the difference in quantum numbers l and m, are also called the **subshell**s.

In the hydrogen-type atomic orbital function in which one electron exists for one nucleus, if the main quantum number is the same, the energy levels of the subshells are the same. However, in a multi-electron atom, there is a repulsion between electrons, and each subshell's energy level becomes different. The 2*p* orbital is at a higher energy level than the 2*s* orbital. Similarly, even within the same electron shell, the energy level rises as the azimuthal quantum number increases in the order of $s \rightarrow p \rightarrow d \rightarrow f$, and the electron becomes unstable. In the subshell, if the azimuthal quantum numbers are the same, the energy levels are generally the same; for example, there is no energy difference in the $2p_x$, $2p_y$, and $2p_z$ orbitals. As the main quantum number n increases, the energy difference between the electron shells becomes smaller, and an orbital with a large azimuthal quantum number has a higher energy level than the higher orbital with a higher main quantum number. The 3*d* orbital has a higher level than the 4*s* orbital, and the 4*f* orbital has a higher level than the 5*p* and 6*s* orbitals. Therefore, the order in which electrons are buried is $1s \rightarrow 2s \rightarrow 2p \rightarrow 3s \rightarrow 3p \rightarrow 4s \rightarrow 3d \rightarrow 4p \rightarrow 5s \rightarrow 4d \rightarrow 5p \rightarrow 6s \rightarrow 4f \rightarrow 5d \rightarrow 6p \rightarrow 7s \rightarrow 5f \rightarrow 6d \rightarrow 7p$. As shown in Fig. 1-4, the electron configuration of an atom can be easily understood by drawing it in a form that is conscious of spin for the energy level of the orbital. Electrons are scattered in as many orbitals as possible, such as the

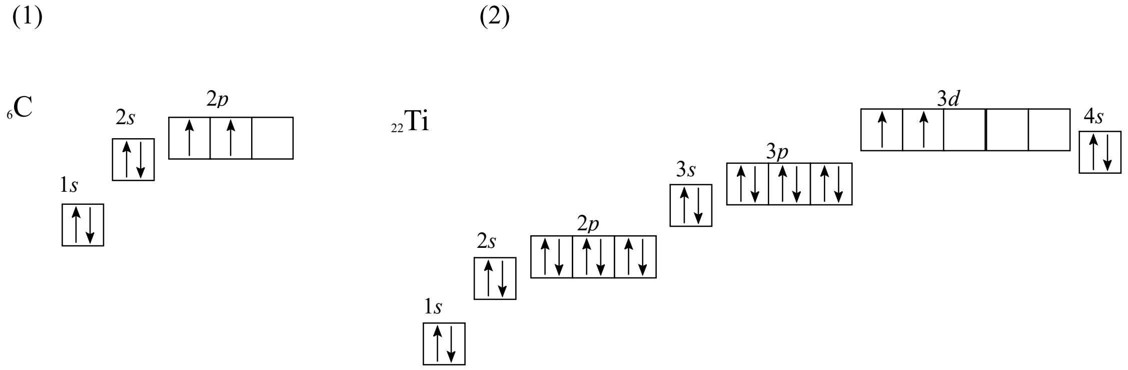


Fig. 1-4 (1) Electron configuration of $_6$C: $1s^22s^22p^2$ (2) Electron configuration of $_{22}$Ti: $1s^22s^22p^63s^23p^63d^24s^2$ (Since the outermost 4*s* orbital has a lower energy level than the 3*d* orbital, electrons enter the 4*s* orbital earlier than 3*d* orbitals.)

3*d* orbitals of the titan atom, so as not to create empty orbitals (unoccupied or vacant) without electrons in the subshell orbitals at the same energy level (**Hunt's rule**). In such atoms, if the spins of odd electrons in semi-occupied orbitals containing only one electron are all in the same direction (α spin), they are stabilised by spin interaction. An electron shell with unoccupied or semi-occupied subshell orbitals is called an open shell, and the atoms of the open shell system work so that each other's electrons fill it and are highly chemically reactive.

The elements on the far right (Group 18) of the periodic table are called noble gases and are known as elements with poor reactivity. An electron shell in which all orbitals are filled with electrons is called a closed shell, and the atoms of Groups 1 and 2 and Groups 12 to 18 in the periodic table (Fig. 1-5) are called main-group elements, in which electrons enter the *s* orbital and the *p* orbitals in order. Since the electron enters the upper *s* orbital before the electron starts to enter the *d* orbital in the electron shell after $n = 3$, the closed shell is up to the *p* orbital, except for the $1s^2$ electron configuration of helium. The outermost shell of noble gas atoms has an electron configuration of s^2p^6. The transition element starts from Group 3 because the upper *s* orbital is first filled, and then the *d* orbital of the inner shell is filled with electrons. Rare earth elements appear after Group 3 in the fifth period because electrons start to enter the 4*f* orbital after the electrons enter the 6*s* orbital. Currently, the officially named element is up to $_{118}$Og (oganesson), but if new elements are synthesised, it will be necessary to consider the next 5*g* orbital ($n = 5$, $l = 4$) after the 5*f* orbital.

Fig. 1-5. Periodic table (2017)

group period	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
I	H																	He
II	Li	Be											B	C	N	O	F	Ne
III	Na	Mg											Al	Si	P	S	Cl	Ar
IV	K	Ca	Sc	Ti	V	Cr	Mn	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se	Br	Kr
V	Rb	Sr	Y	Zr	Nb	Mo	Tc	Ru	Rh	Pd	Ag	Cd	In	Sn	Sb	Te	I	Xe
VI	Cs	Ba	lanthanoid	Hf	Ta	W	Re	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi	Po	At	Rn
VII	Fr	Ra	actinoid	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Nh	Fl	Mc	Lv	Ts	Og

lanthanoid	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
actinoid	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

1-2 Properties of elements, the octet rule, and electronegativity

Chemistry research was active even before the development of quantum mechanics, and the chemical laws known as empirical laws before that were theoretically explained in terms of quantum chemistry derived from quantum mechanics. Gilbert N. Lewis, an American chemist, found from research on chemical bonds that the outermost shell of an atom is stable with eight electrons; this became known as the **octet rule**. As we saw in the previous section, the stable closed shell structure is consistent with the octet electronic state of s^2p^6, in which all electrons are contained in the s orbital and p orbital in the **outermost shell**. The electrons lacking in the octet or the surplus electrons are called valence electrons, and this number is used as the valence, which determines the number of chemical bonds formed when an atom forms a molecule. The outermost-shell orbital that takes in valence electrons is the valence orbital. Lewis showed chemically that valence electrons form an electron pair and stabilise as a molecule, based on Pauli's exclusion principle and have both αβ spins in one orbital. It corresponds to the fact that only two electrons can enter one orbital. The higher the nuclear charge of the nucleus, the stronger the attraction of electrons. In addition, the outermost-shell electron is less affected by the nuclear charge as the electron is in an orbital with a larger main quantum number because the inner-shell electrons block the nuclear charge of the nucleus. As the atomic number increases and the nuclear charge increases toward the right direction of the periodic table, the external electrons are attracted to **unoccupied** and **semi-occupied orbital**s. However, in noble gases, the orbitals that allow electrons to enter exist outside the outermost shell, and the force that attracts new electrons rapidly weakens. The **electronegativity** (Table 1-1) introduced by Linus C. Pauling is a numerical value that compares the ability of an atom to attract more electrons from the outside, and the highest is the halogen element of the second period, fluorine. In the same period, the electronegativity increases as it goes right along the periodic table and goes up in the same group. This is important when considering the **polarity** of chemical bonds between different atoms, which means electronic bias.

Table 1-1. Electronegativity of major elements as defined by Pauling

H	2.2														
Li	1.0	C	2.6	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	Ti	1.5	Cr	1.7	Mn	1.6	Fe	1.8	Cu	1.9	Zn	1.7
Se	2.6	Br	3.0	Ag	1.9	Sn	2.0	I	2.7						

The properties of these elements are related to the energy of electrons in atomic orbitals. Even the electron at the highest energy level of an atom has a lower energy than the free electron in a vacuum. In order to remove an electron from an atom and make it a **cation** with a positive charge of

+1, it requires energy for the amount stabilised by this coulombic force. This energy is called the **ionisation potential**, and although it is a positive value, the value is equal to the value obtained by subtracting the orbital energy of the highest occupied atomic orbital with two electrons or the semi-occupied orbital with one electron from 0 eV. The larger the nuclear charge, the larger the magnitude, and if the period is the same, the element on the right side of the periodic table shows a larger value and becomes the largest in Group 18. In addition, in the same group, the lower the period, the smaller the nuclear charge is blocked by the inner shell electrons, and the ionisation potential is small to form a cation.

Conversely, the energy released when an atom receives an electron to become an **anion** is called **electron affinity**, which is also associated with unoccupied and semi-occupied orbitals. It is the value obtained by subtracting the orbital energy of the highest semi-occupied atomic orbital level or the lowest unoccupied atomic orbital from 0 eV. It is related to the orbital energy of the lowest level of the unoccupied orbitals or the semi-occupied atomic orbital and increasing electron repulsion. If an atom has a semi-occupied orbital with a low energy level, such as a Group 17 element, the value will be large, but if a new electron does not enter a lower-level orbital, such as a Group 18 element, it will be a large negative value. Therefore, an element with a small ionisation potential is an electropositive element and easily forms a cation, and an element with a large electron affinity is electronegative and easily forms an anion (Table 1-2).

Table 1-2. Measured ionisation potential (eV) and electron affinity (eV) of major elements

Element	Ionisation potential	Electron affinity	Element	Ionisation potential	Electron affinity
H	13.598443	0.75419543	He	24.58738	*
Li	5.391719	0.618049	B	8.29802	0.279723
C	11.26030	1.262119	N	14.5341	*
O	13.61805	1.461109	F	17.4228	3.4011895
Na	5.139076	0.547926	Mg	7.646235	*
Al	5.985768	0.43283	Si	8.15168	1.3895220
P	10.48669	0.7465	S	10.36001	2.077103
Cl	12.96763	3.612724	Ar	15.759610	*
K	4.3406633	0.50147	Ca	6.11316	0.02455
Cr	6.76651	0.666	Mn	7.43402	*
Fe	7.9024	0.151	Co	7.88101	0.662
Ni	7.6398	1.156	Cu	7.72638	1.235
Zn	9.394199	*	Se	9.75239	2.020670
Br	11.8138	3.363588	Ag	7.57623	1.302

* Unable to measure because unstable anions are generated.

1-3 Chemical bonds

Substances that exist as single-atom molecules, such as noble gases, are rare, and atoms usually form molecules and exist as compounds. Chemical bonds include **ionic bond**s, **covalent**

bonds, and **metallic bond**s*. However, since metallic bonds are found in uncharged metallic solids via free electrons, the important chemical bonds of biomolecules are ionic bonds and covalent bonds.

Ionic bond

Group 1 and Group 2 atoms, with low electronegativity, have a weak ability to capture electrons in the *s* orbital in the **valence orbital** and donate electrons to atoms with higher electronegativity to generate cations with monovalent or divalent positive charges. Conversely, Group 16 and 17 elements with high electronegativity take electrons into their valence orbitals and form negatively charged anions. Since cations and anions have opposite charges, they are attracted by Coulomb attraction to form an ionic bond. However, the distance between the positive and negative ions is not too close due to the repulsion between electrons and the repulsion between nuclei due to Pauli's exclusion principle, the interatomic distance of the bond is relatively long, and the bonding force is weak. Because the coulombic force between ions exists in a non-directional manner, it forms an ionic crystal such as sodium chloride, where six chloride ions surround a sodium ion and six sodium ions surround a chloride ion. Lewis introduced the Lewis structural formula to represent an octet, which represents the outermost-shell electron pair as two dots ":" (Fig. 1-6). The Lewis structural formula of ionic bonds comprises cations without outermost electrons and octet anions. For the name of a cation, add "ion" to the element name, such as hydrogen ion, lithium-ion, and sodium ion.

On the other hand, for the name of an anion, "ide" is added to the element name, such as hydride ion (H^-), oxide ion (O^{2-}), and chloride ion (Cl^-). Ions can also include several atoms for polyatomic ions such as ammonium ion (NH_4^+), sulfate ion (SO_4^{2-}), hydrogen carbonate ion (HCO_3^-), and dihydrogen phosphate ion ($H_2PO_4^-$). Ionic bonds of polyatomic ions form between the most positive and negative atoms.

Fig. 1-6. Lewis structural formula of ionic bonds

Covalent bond

Main group elements such as carbon that exist in the middle of the periodic table are unlikely to become ions, and to prevent an **open shell structure** valence electrons form bonds so that they form electron pairs. In the Lewis structural formula, a bonding electron pair ":" is written between the atomic symbols to indicate a bonding electron pair shared by two atoms. An electron pair not shared by two atoms is a **lone pair** (unshared electron pair) (Fig. 1-7). Depending on the number of

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*While there is also a classification called a **coordination bond** between a metal ion and a ligand, this should be considered as a covalent bond of ionic components.

shared electrons, there are three types of covalent bonds: a **single bond** that shares two electrons, a **double bond** that shares four, and a **triple bond** that shares six in the case of carbon. Since it has an outermost shell of 4 electrons, 8 electrons can be shared between two carbon atoms from the octet rule, but there is no quadruple bond of carbon atoms.

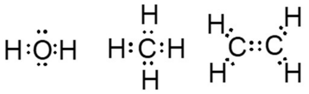


Fig. 1-7. Lewis structural formula of water, methane, and ethene

Bond energy and bond distance

The energy required to break the bond is bond dissociation energy D_e, also called **bond energy**. Assuming that the energy of two atoms at an infinity distance is 0 kJ/mol, as shown in Fig. 1-8, the energy decreases as the distance gets closer. Energy is released (heat generation) by forming a bond, and if it gets too close beyond the interatomic distance of the lowest energy, the repulsive force prevails, and the energy rises again. The interatomic distance R_e at the lowest energy is the equilibrium interatomic distance, which is the **bond distance**. The larger the D_e, the more stable and stronger the bond, C-H bond: 400 to 440 kJ/mol, O-H bond: 460 to 500 kJ/mol, C-C bond: 350 to 380 kJ/mol.

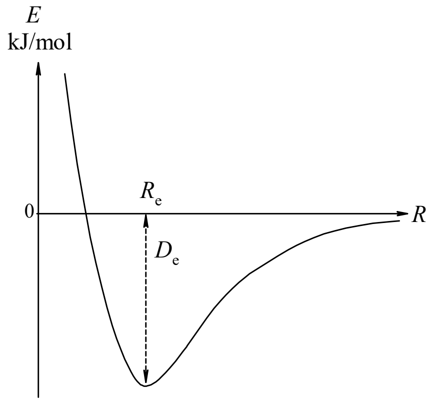
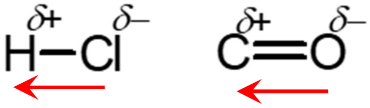


Fig. 1-8. Relationship between bond distance and bond energy

Polarised covalent bond

In a covalent bond between atoms of the same type, such as a bond between two carbon atoms, the two electrons that are bonded are evenly distributed between the two atoms, but if the atom type is different, the bonding electrons will be attracted more strongly to the atom with a high degree of electronegativity. The atom to which a bonding electron pair is attracted with an increased electron density is negatively charged, and the atom with a decreased electron density is positively charged.

This separation of charges is called **polarisation**, and **polarised molecule**s are said to have polarity. Bonds in which the electron pair has completely moved are ionic bonds, but most of them only have partial movement, and the resulting partial charges of the atoms contained in the polarised bond show polarisation at $\delta+$ / $\delta-$ ($0 < \delta < 1$) (Fig. 1-9). Such polarisation causes ionic chemical reactions and **molecular interaction**s. Molecules with polarity have a non-uniform charge distribution with positive and negative charge centres. The molecule will have an electric field vector from the positive charge's centre to the negative charge's centre. The electric field vector in this molecule is called a **dipole moment** and is represented by a vector arrow. The dipole moment vector is drawn from the centre of the negative charge toward the centre of the positive charge*. The larger the charge separation and the further the centre of the charge is, the larger the dipole moment becomes, and its magnitude is expressed in the unit of debye (D). Molecules with a large dipole moment have the property of aligning in parallel with an external electric field in a liquid and increasing the dielectric constant.



dipole moments

Fig 1-9. Polarised covalent bonds

1-4 Orbital interaction and molecular orbital method

In quantum chemistry, how is a chemical bond understood? Considering the case where the hydrogen atom H_A and H_B at infinity approach each other when a hydrogen molecule is formed from two hydrogen atoms, H_A has one electron in the $1s_A$ orbital, and H_B has one electron in the $1s_B$ orbital, although the spins of both are different. At infinity, they do not affect each other. However, as the distance approaches, the H_A electron is attracted to the H_B nucleus, and the H_B electron is also attracted to the H_A nucleus. At the same time, repulsion between nuclei and repulsion between electrons also occur. The Schrödinger equation of such a system can no longer be mathematically solved. Therefore, in an approximate solution called the **molecular orbital** theory, the molecular orbital function Ψ of this system is approximated by the linear combination of $1s_A$ and $1s_B$ as

$$\Psi = c_A 1s_A + c_B 1s_B \qquad (1\text{-}7)$$

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*Many organic chemistry textbooks incorrectly define the orientation of this dipole vector in reverse. If the dipole vector is defined in the opposite direction ($\delta+ \rightarrow \delta-$), the vector direction of the dipole vector and the external electric field becomes antiparallel when the polar molecule is placed in the external electric field.

where the orthonormal condition is satisfied even with this synthesised molecular orbital function Ψ.

Hückel molecular orbital method

In the molecular orbital theory, the best set of molecular, atomic orbital coefficients c_A and c_B are determined by various approximating methods, usually employing numerical integrals. Here, the most primitive approximation method, the **Hückel method**, is used to explain the molecular orbital theory.

When two hydrogen atoms are bonded, a molecule H_2 is formed. What kind of movement does the electron do in this situation? The electron of a hydrogen atom is in the 1*s* atomic orbital under the attraction of coulombic force from the nucleus. Since the H_A and H_B nuclei exist in the hydrogen molecule, the electron e_A belonging to H_A is also attracted by the H_B nucleus when it becomes a molecule. Similarly, the electron e_B is attracted by coulombic force from both the H_A and H_B nuclei. At the same time, there is a Coulomb repulsion due to a positive charge between the nuclei H_A and H_B and a Coulomb repulsion between the electrons e_A and e_B. Expressing such a relationship in the three-dimensional Schrödinger equation as

$$\left(-\frac{\hbar^2}{2m}\nabla^2 + V_{\mathrm{H_A}-e_\mathrm{A}} + V_{\mathrm{H_B}-e_B} + V_{\mathrm{H}_A-e_B} + V_{\mathrm{H}_B-e_A} + V_{e_A-e_B} + V_{\mathrm{H}_A-\mathrm{H}_B}\right)\Psi(x,y,z) = E\Psi(x,y,z) \qquad (1\text{-}8)$$

where $\nabla^2 = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2}$, $V_{\mathrm{X-Y}} = -\frac{Z_\mathrm{X} Z_\mathrm{Y}}{4\pi\varepsilon_0 r}$, and *Z* is the electronic charge of nuclei. Molecular orbital function Ψ is the linear combination of atomic orbitals of 1*s* orbital function (LCAO: eq. (1-7)). Using the Hamiltonian operator, the Schrödinger equation can be written as eq. (1-9).

$$H\Psi = E\Psi \qquad (1\text{-}9)$$

Multiply both sides of this equation by Ψ(*x*, *y*, *z*) from the left to give eq. (1-10).

$$\Psi|H|\Psi = \Psi E\Psi \qquad (1\text{-}10)$$

Integrals of both sides over the entire space ($-\infty < x < \infty$, $-\infty < y < \infty$, $-\infty < z < \infty$) are expressed as eq. (1-11) and eq. (1-12).

$$\langle\Psi|H|\Psi\rangle = \langle\Psi|E|\Psi\rangle \qquad (1\text{-}11)$$

$$E = \frac{\langle\Psi|H|\Psi\rangle}{\langle\Psi|\Psi\rangle} \qquad (1\text{-}12)$$

Appling eq. (1-7) to eq. (1-12), the molecular energy can be expressed as eq. (1-13).

$$E = \frac{< c_A 1s_A + c_B 1s_B |H| c_A 1s_A + c_B 1s_B >}{< c_A 1s_A + c_B 1s_B | c_A 1s_A + c_B 1s_B >} \qquad (1\text{-}13)$$

The Hückel approximation defines the following values:

Coulombic integral: $\alpha = \langle \psi_X | H | \psi_X \rangle$
Resonance integral: $\beta = \langle \psi_X | H | \psi_Y \rangle$
Overlap integral: $S = \langle \psi_X | \psi_Y \rangle$

In these assumptions, no real numerical values are treated, while the coulombic integral α is the orbital energy of 1*s* orbital of hydrogen. From the normalised conditions of wave functions, the integral of the square of a wave function is equal to 1 as eq. (1-14).

$$\langle \psi_X | \psi_X \rangle = 1 \qquad (1\text{-}14)$$

Thus, eq. (1-13) can be rewritten as eq. (1-15) and eq. (1-16).

$$E = \frac{(c_A^2 + c_B^2)\alpha + 2c_A c_B \beta}{(c_A^2 + c_B^2) + 2c_A c_B S} \qquad (1\text{-}15)$$

$$E\{(c_A^2 + c_B^2) + 2c_A c_B S\} = (c_A^2 + c_B^2)\alpha + 2c_A c_B \beta \qquad (1\text{-}16)$$

In the simple Hückel method, which is the roughest approximation, the overlap integral *S* is treated as equal to 0. When the combination of c_A and c_B is the most appropriate, the molecule's energy should be the lowest (variational principle). Therefore, in this combination, the energy *E* should be the minimum value, and if eq. (1-16) is partially differentiated by c_A and c_B, respectively, the partial differential term of energy *E* becomes 0, and the simultaneous equations with three unknowns (c_A, c_B, and *E*) eqs. (1-17) and (1-18) are obtained.

$$c_A(\alpha - E) + c_B \beta = 0 \qquad (1\text{-}17)$$

$$c_A \beta + c_B(\alpha - E) = 0 \qquad (1\text{-}18)$$

Mathematically, the condition for these equations to have a solution other than $c_A = 0$ and $c_B = 0$ is the following determinant eq. (1-19), called the secular determinant, must be 0.

$$\begin{vmatrix} \alpha - E & \beta \\ \beta & \alpha - E \end{vmatrix} = 0 \qquad (1\text{-}19)$$

Eq. (1-19) can be written as the secular equation eq. (1-20).

$$(\alpha - E)^2 - \beta^2 = 0 \qquad (1\text{-}20)$$

Eq. (1-20) has two solutions, E_1 and E_2, and the coefficients c_A and c_B of each orbital can be obtained by substituting into eq. (1-17) and eq. (1-18), and since $c_A^2 + c_B^2 = 1$ from the normalised conditions, eq. (1-21) and eq. (1-22) are obtained.

$$E_1 = \alpha + \beta : \quad \Psi_1 = \frac{1}{\sqrt{2}}(1s_A + 1s_B) \tag{1-21}$$

$$E_2 = \alpha - \beta : \quad \Psi_2 = \frac{1}{\sqrt{2}}(1s_A - 1s_B) \tag{1-22}$$

Here, since α and β are smaller than 0 because they are stabilisation energies, E_1 is smaller than E_2. If overlap integral S is not ignored, E_1 (E_+), E_2 (E_-), Ψ_1 (ψ_+), and Ψ_2 (ψ_-) are written as follows:

$$E_+ = \frac{\alpha + \beta}{1 + S} \qquad \psi_+ = \frac{1}{\sqrt{2(1+S)}}(1s_A + 1s_B) \qquad E_- = \frac{\alpha - \beta}{1 - S} \qquad \psi_- = \frac{1}{\sqrt{2(1-S)}}(1s_A - 1s_B) \tag{1-23}$$

Integrals β and S are dependent on the interatomic distance. When two atoms are closer, the energy E_+ decreases, the ψ_+ is stabilised, while the energy E_- increases and the ψ_- is destabilised. Figure 1-10 is the **orbital energy diagram**, and the vertical scale represents the orbital energy level. This shows the changes in orbital energies of 1*s* when a hydrogen molecule forms from two hydrogen atoms. The **orbital interaction** occurs when two orbitals approach each other and split into stable and unstable orbitals. Since the hydrogen molecule has two electrons, it is more stable than the state in the atomic 1*s* orbital by entering the ψ_+ orbital of the low energy level by Pauli's exclusion principle. The bond energy is the energy stabilisation (2 × ΔE) for two electrons. What is the shape of the molecular orbitals? The lower energy ψ_+ is the sum of the two 1*s* orbital functions. Therefore, the electron density is higher in the space between two hydrogen atoms than in the original 1*s* orbital.

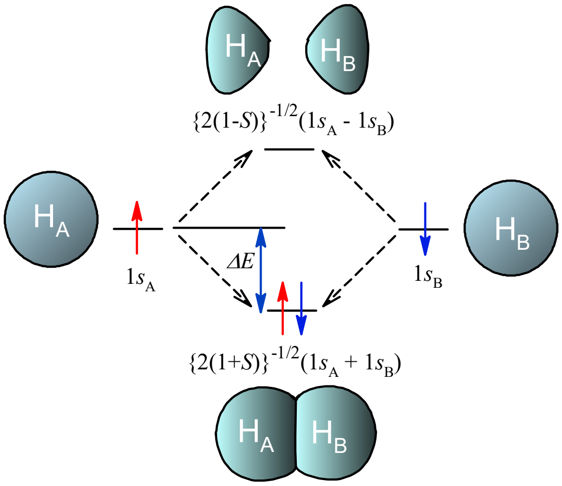

Fig. 1-10. Orbital energy diagram of hydrogen molecule: Two electrons enter a low energy level bonding molecular orbital to form a stable molecule.

Instead, the electron density is relatively reduced on the opposite side of each atom. Since the electron density increases in the partial bonding region, this orbital is called a **bonding orbital**.

On the other hand, the higher-energy ψ_{-} is the difference between the two 1*s* orbital functions. Therefore, there is a node where the electron density becomes 0 at the position between both hydrogen atoms. Since there are no electrons in the bonding region and it is unstable, such an orbital is called an **anti-bonding orbital**. Helium, a noble gas element, does not form diatomic molecules like hydrogen. When a helium atom with two 1*s* electrons approaches each other, it splits into two orbitals, ψ_{+} and ψ_{-}, as in the case of a hydrogen atom. Since it has 4 electrons, it is necessary to put electrons into the destabilised anti-bonding orbital ψ_{-} and the stabilised bonding orbital ψ_{+}. When the atoms get closer, the destabilisation by the nuclear repulsion causes the diatomic molecule to become unstable, and the molecule He_2, without electronic stabilisation, cannot be formed. The orbital function obtained by the molecular orbital method shows the spread of electrons in a hydrogen molecule and represents the molecule's electron density.

A linear combination of atomic orbitals created the molecular orbitals $\psi\pm = c_A 1s_A \pm c_B 1s_B$. From the normalised condition of the wave function, the integral over the total space of ψ^2 is $c_A^2 + c_B^2 = 1$ if the assumption of $S = 0$ of the simple Hückel method is accepted. Since c_A^2 and c_B^2 represent the probability that an electron exists around H_A and H_B, they represent the electron density at each atom. In the case of a hydrogen molecule, $c_{A+}^2 = c_{B+}^2 = 0.5$ of the bonding orbital ψ_{+}, and since there are two electrons in ψ_{+}, it is shown that one electron belongs to each atom. Also, in the case of a multi-electron atom, the number of molecular orbitals increases, and the sum of the squares of these atomic orbital coefficients gives the total electron density of the atom. If this total electron density is subtracted from the number of nuclear charges $+Z$, the total number of atom charges, the partial charge δ+ or δ– generated by polarisation, can be calculated. In the case of a hydrogen molecule, there is no difference in energy level between the two atomic orbital functions, and there is no bias in the electron density or the total charge in the bond. However, there is a difference in c_A and c_B in the bond between different atoms.

In the bonding orbital, the coefficient on the side of the atomic orbital with a low energy level is large, and conversely, the coefficient on the side of the atomic orbital with a high energy level is small, and a difference in electron density is formed between the two atoms. Since an atom with a large electronegativity has a large positive charge in the nucleus, the energy of the Coulomb attraction with an electron is also large, and the energy level of its atomic orbital is low. When solved by the molecular orbital method, the coefficient on the side with the larger electronegativity becomes larger. In a polarised bond, there is a difference between c_{A+}^2 and c_{B+}^2, which indicates the partial charges δ+ and δ– of the polarised atom. Also, looking at the coefficients of the anti-bonding orbitals that do not contain electrons, the electron densities are opposite because the total electron densities of the

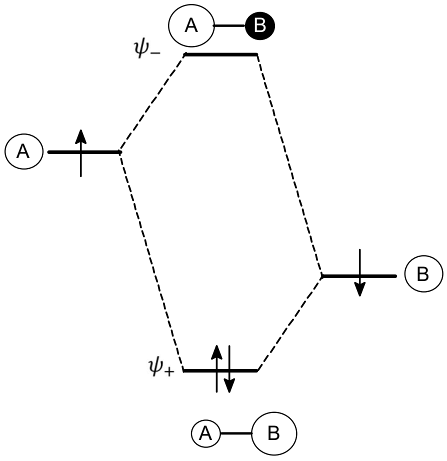

Fig. 1-11. Orbital diagram of A-B bond between two atoms with different electronegativity: In the bonding orbital, the distribution of lobe spreads to the atom with high electronegativity, and in the antibonding orbital, it spreads to the atom with low electronegativity.

bonding orbital of atom A and the anti-bonding orbital $c_{A+}{}^2 + c_{A-}{}^2$ are equal to 1. Figure 1-11 shows a schematic orbital energy diagram of such a bond. The energy levels of bonding orbitals and anti-bonding orbitals of the single bond consisting of an atom A with lower electronegativity and an atom B with higher electronegativity, and the magnitude of their coefficients c_{A+}, c_{A-}, c_{B+}, and c_{B-} are indicated by open circles and a black circle. The colour difference indicates the difference in the sign (phase) of the atomic orbital coefficient c, and the magnitude indicates the magnitude of the absolute value of the coefficient. Since the electron density is the square of the coefficient, it also represents the electron density whose magnitude is localised in each atom.

Previously, δ+ and δ–, which represent the partial charges of a polarised bond, had only a descriptive meaning, but with the molecular orbital method's introduction, the polarisation magnitude has become a concrete numerical value (Fig. 1-12).

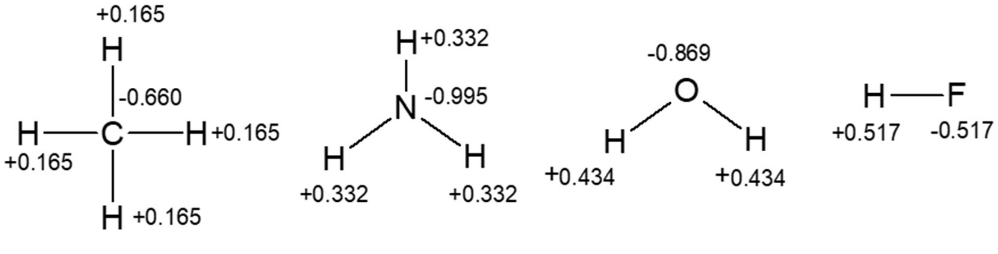

Fig. 1-12. Atomic charges of a simple molecules (*ab initio* 6-31G*-calculated Mulliken charge density): The higher the electronegativity of the central atom, the larger the positive charge of the bonding hydrogen.

1-5 σ Bond / π bond and hybrid orbital

Since the *s* orbital has no directionality, there is only one bonding mode for hydrogen molecules. On the other hand, since the *p* orbital has anisotropy in the spatial spread of the orbital, there are two different types of coupling modes depending on the direction in which the orbitals approach. For example, a bonding mode in which $2p_x$ orbitals approach along with the *x*-axis direction is called **σ bond** (Fig. 1-13 (a)), and in the other mode, they approach in parallel from the *y*-axis direction. This bonding mode is called **π bond** (Fig. 1-13 (b)). In both bonding orbitals, the electron density in the interatomic region increases due to the sum of the orbital functions, as in the case of hydrogen, showing stable bonding, but the σ bond has a larger orbital overlap and is stronger. Since the orbital interaction occurs and the range of change in the orbital energy level is large, the energy range of the splitting of the molecular orbital is large, and the bond is stable. Therefore, the relationship between the bond energies $D_{e\sigma}$ and $D_{e\pi}$ is always $D_{e\sigma} > D_{e\pi}$ if the bonding atoms are the same.

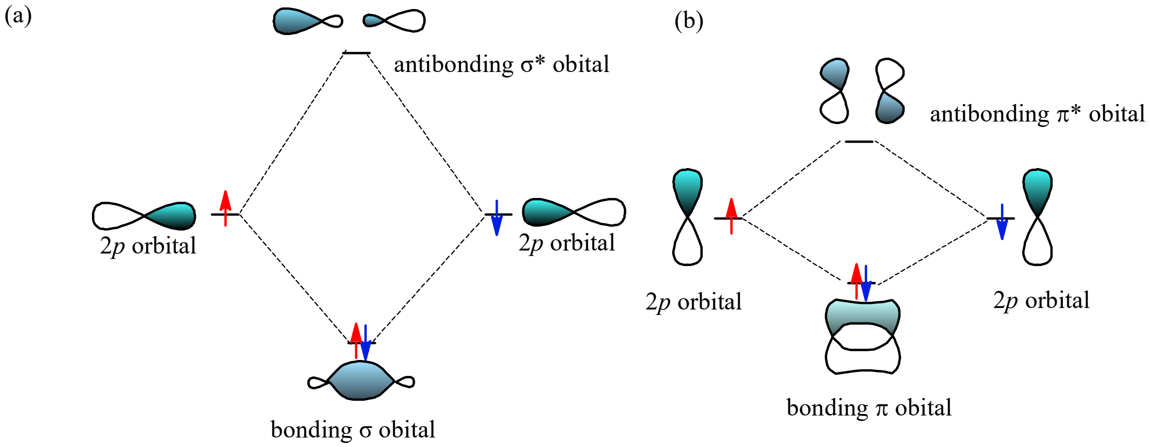

Figure 1-13 (a) σ bond of 2*p* orbital (b) π bond of 2*p* orbital: Add an asterisk (*) to the antibonding orbitals.

Although the σ bond is a stable orbital, the interaction between the 2*s* orbital and the 2*s* orbital and the σ-type interaction between the 2*p* orbital and the 2*p* orbital have limited orbital overlap.

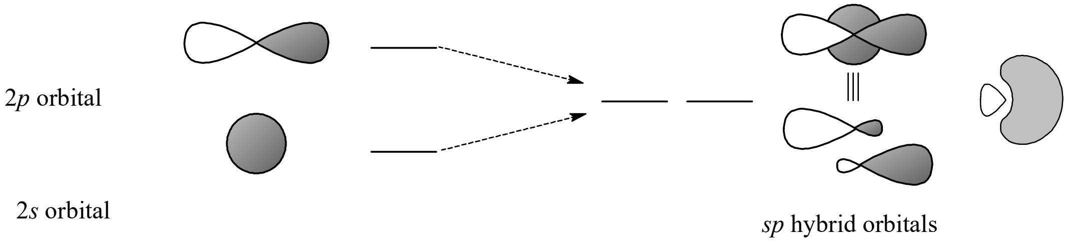

Fig. 1-14. Formation of *sp* hybrid orbitals: By averaging 2*s* and 2*p* orbitals, two *sp* hybrid orbitals with spatially biased electron densities are created.

Pauling proposed a hybrid orbital model as a hypothetical method of understanding how to redistribute atomic orbitals to increase stabilisation when σ bonds are formed. Within one atom, the 2*s* orbital and the 2*p* orbital are close to each other and can be fused to redistribute the electron distribution. A linear combination of orbital functions can create a hybrid orbital by adding coefficients to meet the normalisation conditions. The 2*s* orbital function has the same sign in all directions, while the 2*p* orbital function has positive and negative signs depending on the direction of the orbital axis. If the sum or difference is taken, the function value will increase or decrease depending on the direction. This redistribution of orbitals is the hybrid orbital and causes a spatial bias in the orbital values. The two lobes in the original 2*p* orbital change to the larger part where the electron distribution is biased and the smaller part. In particular, this smaller lobe is called the back lobe (Fig. 1-14).

For example, when a 2*s* orbital and one 2*p* orbital are mixed, an *sp* hybrid orbital is formed (Fig. 1-15 (a)). The energy level of the hybrid orbital formed is the average of the energies of the 2*s*

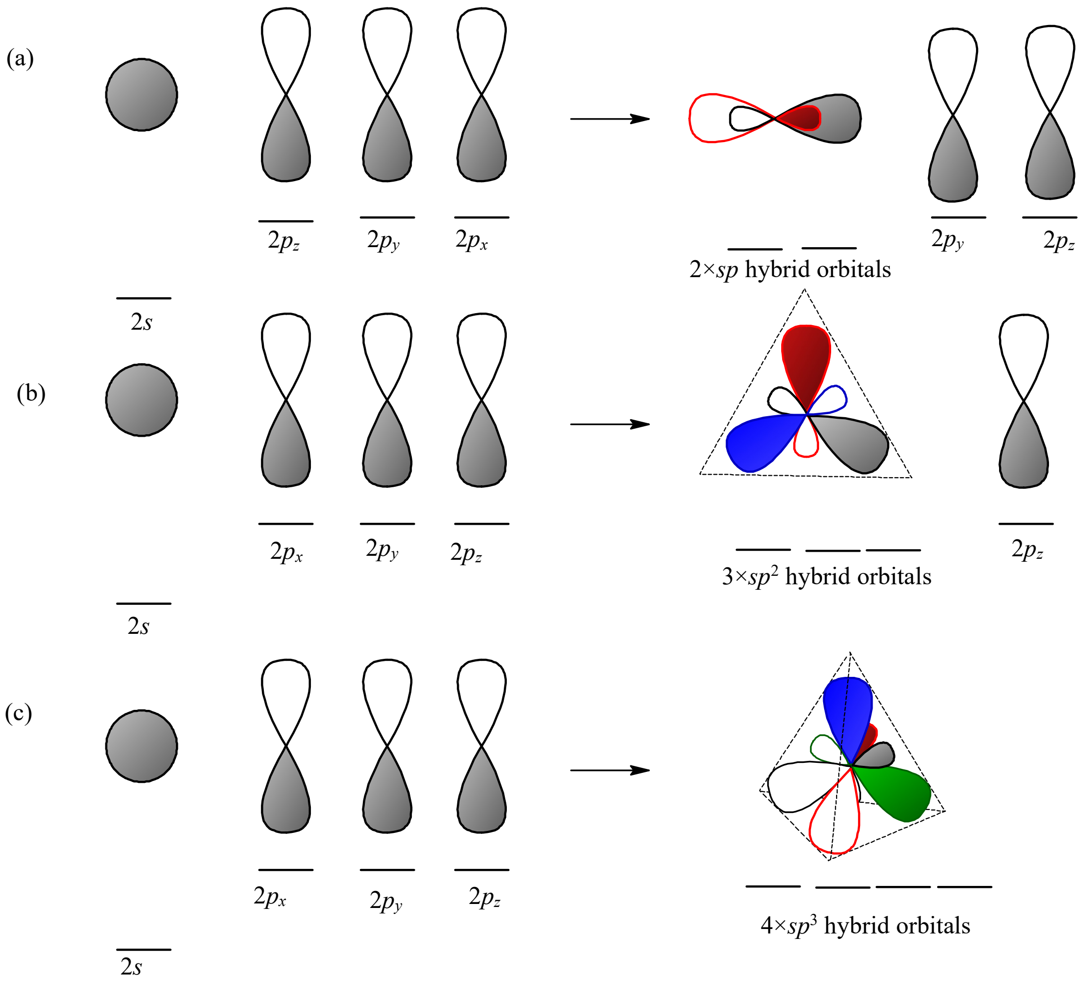

Fig. 1-15. Formation of hybrid orbitals by 2*s* and 2*p* orbitals: (a) *sp* hybrid orbitals, (b) sp^2 hybrid orbitals, (c) sp^3 hybrid orbitals.

orbital and the 2*p* orbital, and there must also be two hybrid orbitals formed when the two orbitals are mixed to satisfy the Pauli's exclusion principle. Also, the spatial arrangement of the electrons must coincide with the region where the first 2*s* orbital and the 2*p* orbital are added. At first glance, it seems that the spatial spread of the hybrid orbital does not match the distribution of the 2*s* and 2*p* orbitals, but the correct form of the hybrid orbital is shown on the right in Fig. 1-14. The σ bond on the side of the large lobe allows stronger interaction than the σ bond of the non-hybridised orbital, forming a stronger bond. The two *sp* hybrid orbitals are symmetrical, and the two large and small lobes of each are orientated in opposite directions to the nucleus. Since the σ bond can be formed in the orbital axis direction, the molecule containing the *sp* hybrid diatomic bond becomes a linear molecule with a bond angle of 180°.

Similarly, the three sp^2 hybrid orbitals are formed from the 2*s* orbital and the two 2*p* orbitals, and since each σ bond points in three directions on a plane, the bond angle is 120°, and its orbital energy level is the average of the 2*s* orbital and the two 2*p* orbital energies (Fig. 1-15 (b)). When the 2*s* orbital and all 2*p* orbitals are mixed, four sp^3 hybrid orbitals are formed. Since all three-dimensional space is used, the formed hybrid orbital lobes direct to the tetrahedron's four vertexes and the bond angle is 109.5°. The orbital energy level is the average of the 2*s* orbital and the three 2*p* orbital energies (Fig. 1-15 (c)). The valence electrons of a carbon atom are four and have an electron configuration of $2s^22p^2$, but when four sp^3 hybrid orbitals are formed, one electron in the 2*s* orbital must be transferred to the high-energy 2*p* orbital. However, the orbital hybridisation stabilises the carbon atom since four stable bonds σ are formed. Since the hybrid orbital model treats the σ bond as a localised bond, it is considered that the four bonds are equivalent. The four hydrogens of methane are equivalent and indistinguishable, but the eight electrons in the σ bonds (C–H bonds) are not equivalent. The molecular orbitals of the formed σ bonds consist of three **degenerated orbitals** of equal orbital energy and one lower-energy orbital. Namely, 6 out of 8 σ-bonded electrons have high energy and 2 electrons have low energy. This can be seen by analyzing the entire methane molecule by the molecular orbital method, and the hybrid orbital model is considered from a different approximation method of quantum chemistry called the valence bond method. The properties look different from the molecular orbital method, but both are correct depending on the approximation methods. It also shows that the carbon atom changed from the $2s^22p^2$ arrangement in the atomic state to the $2s^12p^3$ arrangement when it changed to the molecular state.

1-6 Chemical bonds and molecular shapes

In organic chemistry, the composition of a molecule is expressed using a molecular formula that summarises the number of constituent atoms and a structural formula that describes the arrangement of atoms. The molecular formula shows the elemental symbol of the atom contained in the molecule and the atom numbers, which are arranged in alphabetical order, but carbon and hydrogen, which are important in organic compounds, are in front and written as $C_nH_mA_xB_y$. Compounds that have the same molecular formula but have different physical properties and can be recognised as different types of substances are called **isomer**s, and they have a structural formula such as $CH_3CH(OH)CH_2C(=O)CH_2COOCH_3$. In addition to the **structural isomer**s that can be identified when the formula is written in one line, there are ***cis-trans*** **isomer**s and **stereoisomer**s, which will be described later. The arrangement of covalent bonds between the atoms of a molecule is expressed by a **structural formula** written in several forms of expression (Fig. 1-16). This is a formula in which the bonding electron pair of the Lewis structural formula is drawn with a bond line, and the lone pair is excluded. The carbon atom of sp^3 hybridisation has a tetrahedral three-dimensional structure, but the structural formula is expressed in a plane. Complex molecules with many carbon atoms are drawn by omitting carbon and hydrogen bonded to carbon. There is a carbon atom at the intersection of the fold and branch of the straight line with the end, and if there are fewer than four bond lines, it indicates that the rest is connected to hydrogen. Often, some people omit only hydrogen, but this is incorrect. If C is marked, H must not be omitted. When describing a three-dimensional structure, a wedge-shaped connection line or a broken line connection line indicates the steric arrangement of the atoms. The wedge-shaped or boldface bond line represents the bond with the atom above the paper surface, and broken lines represent the bond with the atom under the paper surface, respectively. (Fig. 1-17). Computer software on the market makes drawing complex structural formulas easy.

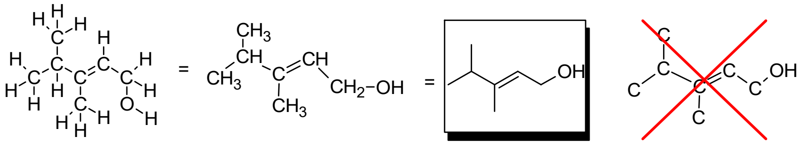

Fig. 1-16. Structural formulas of various expressions. The element symbols C and H for carbon and hydrogen may be omitted at the same time, but H must not be omitted when C is written.

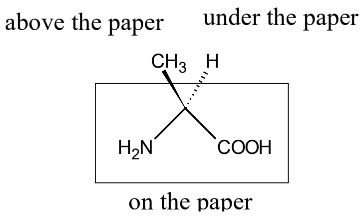

Fig. 1-17. Three-dimensional structural formula of alanine.

An important index for considering structural isomers from the molecular formula is the **degree of unsaturation** Ω, which determines the number of substructures such as double bonds, triple bonds, or cyclic structures from the molecular formula. In the saturated acyclic organic compounds, Ω is equal to 0. If a molecule has a molecular formula of $C_aH_bN_cO_dX_e$, where X is a halogen atom, the degree of unsaturation Ω is calculated as eq. (1-23). The degree of unsaturation increases by one if the molecule has a double bond or a cyclic structure, but the degree of unsaturation