ISOTOPE EFFECTS, ISOTOPE SEPARATION AND ISOTOPE FRACTIONATION

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Contents

Summary

Isotope effects in spectroscopy, chemical equilibria, phase equilibria, physicochemical properties, reaction kinetics, and biology are discussed. To understand the experimentally observed isotope effects the basics of the theory of isotope effects is treated at an elementary level. Different isotope separation processes, which are used to enrich stable isotopes, are described. The large-scale methods of heavy water production and ^{235}U isotope enrichment are outlined in some detail. Finally the mechanisms of isotope fractionation in nature, the variations of stable isotope compositions and some of their applications are discussed.

1. Introduction

If naturally occurring water, containing deuterium (i.e. hydrogen-2, ^{2}H, to be denoted by D) in low concentration, evaporates then the concentration of deuterium in the liquid phase increases because H_2O is more volatile than HDO. The viscosity of heavy water (D_2O) is higher than that of H_2O. The diffusion rate of ^{36}Ar isotope is higher than that of the heavier argon isotope ^{40}Ar. The infrared spectrum of methane (CH_4) is different from that of deuteromethane (CD_4). The equally charged ions of ^{63}Cu and ^{65}Cu are accelerated to different velocities by the same electric potential. The reaction of an organic compound becomes substantially slower if, in the bond which is broken during the reaction, hydrogen is replaced by deuterium (e.g. a $C-D$ bond is being broken instead of a $C-H$ bond).

These differences brought about by isotopic substitution in the physical and chemical properties of atoms and molecules are called *isotope effects*. Note that the differences in the characteristic parameters of nuclear transformations (half-life, energy of radiation, cross section) are not considered as isotope effects. Molecules which differ in their isotopic composition are called *isotopic molecules*. According to the IUPAC terminology, a molecular entity that differs solely in isotopic composition (number of isotopic substitutions), e.g. CH_4, CH_3D, CH_2D_2, CD_4 should be properly called *isotopologue*; however, this terminology is not widely used. Another term one can find occasionally in the literature is *isotopomers*; these are molecules which contain the same number of each isotopic atom but in different positions (e.g. $CH_2DCH{=}O$ and $CH_3CD{=}O$).

Isotope effects are usually based on the differences between the masses of the atoms and therefore they are referred to sometimes as 'isotope-mass effects' (the so-called 'mass-independent isotope effects', e.g. the 'magnetic isotope effects' which are due to the differences between the nuclear spins of isotopes, will be described in Section 2.7). The geometrical and electronic structures of isotopic molecules are very nearly the same because isotopic nuclei differ only in the number of neutrons, while it is the number of protons which determines the nuclear charge and thus the electron distribution and molecular structure. This fact leads to a great simplification in interpretation and theoretical calculations of isotope effects.

Isotope effects can be divided in two main groups: phenomena which are directly connected to the differences in the molecular mass (thermal motion, motion in gravitational, electric and other fields) and those connected to different mass distributions within the molecule (isotope effects on molecular spectra, chemical equilibria, rate of chemical reactions etc.). Isotope effects may also be classified according to the field in which they are observed: physics, chemistry, biology, geology, spectroscopy etc. The differences in chemical and physical properties of the isotopes form the basis of their separation from each other and make possible the production of enriched isotopes for industrial, military, medical and research purposes. The various isotope effects on physical, chemical, geological and biological processes lead to isotopic fractionation in nature and thus to the variation of stable isotope compositions of various elements (hydrogen, oxygen, carbon, etc.). The systematic investigation of these variations can be applied to the determination of the origin of natural formations, geothermometry, food authentication etc.

2. Isotope Effects

2.1. Mechanical Effects

The average speed of gas molecules at a given temperature depends on their masses, therefore, in a gas made up of molecules containing different isotopic species, those molecules containing the light isotope will, on average, have speeds higher than those which contain the heavy isotope. In the gaseous diffusion process used for the separation of the fissile $^{235}\mathrm{U}$ isotope from the far more abundant uranium isotope $^{238}\mathrm{U}$, uranium hexafluoride gas is pushed through a filtration barrier or membrane (see Section 3.1). The lighter $^{235}\mathrm{UF}_6$ molecule will travel slightly faster through the membrane than the $^{238}\mathrm{UF}_6$ molecule. The maximal theoretical separation that can be achieved is equal to the square-root of the ratio of the masses of the gas molecules if the pore size of the membrane is much smaller than the mean free path of the molecules in the gas phase. In the diffusion process for the $^{235}\mathrm{UF}_6/^{238}\mathrm{UF}_6$ separation this ratio is 1.0043. Because this number is so close to unity, the degree of enrichment which can be achieved in a single diffusion stage is very small, but the effect can be multiplied by making use of a cascade consisting of a number of stages (Section 3).

Isotope effects can also be observed in the concentration distribution of gaseous substances in mechanical fields. In the earth's gravitational field, the pressure decreases with increasing altitude which can be described by the barometric formula

$$p_h = p_0 \exp\left(-\frac{Mgh}{RT}\right) \qquad (1)$$

where p_h and p_0 are the pressures at altitude h, and at zero altitude, respectively, g is the gravitational acceleration, M is the molar mass, R is the gas constant and T is the temperature. [It should be noted that during the derivation of Eq. (1) the h dependence of T and g has been neglected, and therefore it is only a rough approximation to actual atmospheric pressures.] As a consequence of Eq. (1), the ratio of the concentrations (c'_h / c_h) of two isotopic variants with molecular masses M' and M, respectively, changes with the altitude according to the following equation

$$\frac{c'_h}{c_h} = \frac{c'_0}{c_0} \exp\left(-\frac{(M - M')gh}{RT}\right) \qquad (2)$$

By using this equation one obtains that the $^{16}\mathrm{O}_2/^{18}\mathrm{O}_2$ isotope ratio of the oxygen in the air at an altitude of 10 km can be expected to be about 9% higher than that at the surface of the earth (the actual difference is smaller due to air convections).

Similarly, the ratio of the concentrations of the two isotopic species will be different at the axis of a gas centrifuge and at a distance r from the axis:

$$\frac{c'_r}{c_r} = \frac{c'_0}{c_0} \exp\left(-\frac{(M - M')(\omega r)^2}{2RT} \right) \qquad (3)$$

where ω is the angular velocity of the centrifuge. The magnitude of the isotope separation factor $[\alpha = (c'_r / c_r)/(c'_0 / c_0)]$ in the centrifugation is the function of the absolute mass difference between the isotopic molecules, not of the relative mass difference which is the case in most other processes. This fact is especially advantageous for isotope separation of heavier elements and centrifugation is widely utilized in the enrichment of ^{235}U isotope (see Section 3.1).

In electric and magnetic fields the deflection of ions from the original direction of motion also depends on their mass m. The deflection (X) of an ion with speed u and charge q in an electric field E can be given as

$$X \propto \frac{Eq}{mu^2} \qquad (4)$$

The magnitude of the deflection (Y) caused by a magnetic field of magnetic flux density B is

$$Y \propto \frac{Bq}{mu} \qquad (5)$$

Equations (4) and (5) show that the deflections of the ions of the lighter isotope are greater than those of the heavier isotope provided their velocities and charges are the same. Isotope analysis by mass spectrometry and the electromagnetic isotope separation method using large-scale mass spectrometers are based on these effects.

The kinetic theory of gases yields theoretical expressions for the thermal conductivity and viscosity of gases. For ideal gases around atmospheric pressure, where the mean free path of the gas molecules is much less than the smallest dimension of the container, the ratio of the thermal conductivities of the isotopic molecules is inversely proportional to the ratio of the square-roots of their molecular masses and does not depend on the pressure of the gas. (At lower pressures, where the mean free path becomes comparable to, or larger than the dimensions of the container, the thermal conductivity will be strongly pressure dependent.) The isotope analysis of isotopic gas mixtures by using a catharometer is based on the fact that, to a first approximation, the relationship between the thermal conductivity and isotopic composition of the mixture is linear. The isotope ratio of the viscosities of gases, but not that of liquids, is equal, in a good approximation, to the square-root of the molecular mass ratio.

On the basis of the mass dependence of the motions of isotopic molecules one can expect isotope effects also in the rate of evaporation, condensation, dissolution and crystallization as well as in electric mobility of ions

2.2. Isotope Effects in Spectroscopy

Isotope effects in spectroscopy are nicely illustrated using the example of the visible spectra of hydrogen which led Urey, Brickwedde and Murphy in 1932 to the discovery of deuterium, the stable heavy isotope of hydrogen with mass number 2. The first public announcement of the discovery was made at the 1931 Christmas meeting of the American Association for the Advancement of Science in New Orleans. Three years later this discovery earned Urey a Nobel price in chemistry. The wavelengths of the spectral lines in the visible spectra of hydrogen can be calculated by the Balmer series formula which describes the energy change accompanying the jump of an electron from the *n*th orbit to the 2nd

$$\frac{1}{\lambda_{\mathrm{H}}} = R\left(\frac{1}{2^2} - \frac{1}{n^2}\right), \quad (n > 2) \tag{6}$$

where λ_{H} is the wavelength of a spectral line, R is the Rydberg constant which depends on the mass of the nucleus; its values for hydrogen and deuterium are $109677.58\ \mathrm{cm}^{-1}$ and $109707.42\ \mathrm{cm}^{-1}$, respectively. Urey and his coworkers observed weak satellites for four of the Balmer lines of hydrogen ($n = 3\ldots6$) which were shifted to shorter wavelengths and the magnitudes of these shifts were found to be in exact agreement with the predictions of Eq. (6) if one assumed the existence of a nucleus with a “mass” of ‘2’. In the first, and most intense line in the Balmer spectrum, which is deep red in color, even the splitting of the deuterium line into a doublet was observed, as was to be expected from theory. It should be remembered that the neutron was unknown at the time of the discovery of deuterium.

In a diatomic molecule isotope effects appear in the vibrational, rotational and electronic spectra. Isotope effects on vibrational-rotational spectra can be interpreted on the assumption that the potential energy surface for the vibrational-rotational motions of a molecular system depends on the nuclear charges of the substituent atoms and on the number of electrons in the system but is independent of the masses of the nuclei. The assumption of an isotope independent potential energy (Born–Oppenheimer approximation**)** is a very important one and is the cornerstone of most theories dealing with the effects of isotopic substitution on molecular properties. Then the harmonic vibrational frequencies of the two isotopic variants of a diatomic molecule (prime denotes the lighter molecule) can be given as

$$\frac{\nu'}{\nu} = \sqrt{\frac{\mu}{\mu'}} \tag{7}$$

where ν is the frequency and μ is the reduced mass [$= m_{\mathrm{a}} m_{\mathrm{b}} /(m_{\mathrm{a}} + m_{\mathrm{b}})$, where m_{a} and m_{b} are the atomic masses of the atoms in the diatomic molecule]. It can be shown that the isotopic shift of the rotational lines is proportional to the ratio of the reduced masses. The rotational lines can be observed in the far infrared region and the rotational spectra can be used for the determination of bond lengths in molecules.

The effect of isotopic substitution appears also in the electronic spectra of diatomic molecules, which led to the discovery of ^{18}O, ^{17}O, ^{13}C, and ^{15}N isotopes by the methods of optical molecular spectroscopy in 1929.

Isotopic substitution plays an important role in the determination of the force field or potential field for small polyatomic molecules. The force field ("force constants") can be determined from the observed vibrational frequencies, as determined from the infra-red and Raman spectra. In the most general case in the force field of an N-atomic non-linear molecule there are ½ $(3N - 6)$ $(3N - 5)$ force constants, but a maximum of only $3N-6$ vibrational frequencies can be observed. Isotope substitution changes the vibrational frequencies without changing the force constants (within the Born–Oppenheimer approximation) and thus increases the number of data from which the force constants can be determined.

The difference in color between heavy water and ordinary water is the manifestation of the isotope effect in vibrational transitions. It is known that pure water and ice are not colorless but have an intrinsic color of pale blue which is due to the absorption of water in the red regions of the visible spectrum thus imparting a cyan color, the complementary color of red, to the transmitted light. The red absorption originates from vibrational transitions and can be ascribed to high energy vibrational overtone and combination bands. In contrast, the absorption of heavy water (D_2O) in the red end of the spectrum is quite small; therefore heavy water can be expected to be colorless. The increase in mass caused by the substitution of deuterium for hydrogen in water results in lower vibrational energies (e.g. the antisymmetric stretching vibration which is at about 3500 cm^{-1} in liquid H_2O shifts to about 2500 cm^{-1} in D_2O), consequently a minimum of six stretching quanta would be required for any absorption in the visible region.

Isotopic substitution can create asymmetry in a molecule. For instance, by replacing one of the hydrogen atoms in a compound of the type $R_1\text{-}CH_2\text{-}R_2$, a chiral molecule is formed that shows optical activity. In this case the molecular chirality arises solely from an isotopic substitution. One example is the α-deuteroethyl benzene molecule in which one of the hydrogen atoms of the methylene group is replaced by deuterium. The optical activity of this compound is $\alpha_D^{25} = -0.30°$.

The isotope effects observed in different spectral regions are often used for isotopic analysis. For example, the IR absorption intensity of the OH-stretching vibration of HDO at 3500 cm^{-1} makes possible the high precision deuterium analysis of heavy water. On the other hand, the intensity of the OD-stretching vibration of HDO at 2510 cm^{-1} can be used for the determination of deuterium content of natural water samples.

There is also a considerable difference between the values of the index of refraction of H_2O and D_2O, 1.33250 and 1.32796 (at 25°C, Na D-line), respectively. This difference can be used for a rapid, although not very precise (±0.4 atom% of D) deuterium analysis of water samples by means of a simple immersion refractometer.

2.3. Isotope Effects in Chemical Equilibria

One of the most characteristic manifestations of the chemical differences between isotopic molecules is the difference between the equilibrium constants for a given chemical reaction. Let us compare the following chemical equilibria:

$$\mathrm{AX}' + \mathrm{BY} = \mathrm{BX}' + \mathrm{AY}$$
$$\mathrm{AX} + \mathrm{BY} = \mathrm{BX} + \mathrm{AY}$$

where X and X' are different isotopes (the prime denotes the lighter isotope). The equilibrium constants can be written as

$$K'_{\mathrm{A}} = \frac{[\mathrm{BX}'][\mathrm{AY}]}{[\mathrm{AX}'][\mathrm{BY}]} \qquad (8)$$

$$K_{\mathrm{A}} = \frac{[\mathrm{BX}][\mathrm{AY}]}{[\mathrm{AX}][\mathrm{BY}]} \qquad (9)$$

where [ ] denotes the concentration. If there were no difference between the chemical properties of the isotopic molecules, then K'_{A} would be equal to K_{A}. However, the vibrational frequencies and, consequently, the zero-point energies and dissociation energies of isotopic molecules are different; therefore the equilibrium constants of the above reactions are also different. The deviation of $K'_{\mathrm{A}} / K_{\mathrm{A}}$ from unity is the isotope effect on the equilibrium constant.

The isotope effect on chemical equilibria can be illustrated with the example of acid-base equilibria. Consider the ionization reactions of the weak acids HA and DA in water and heavy water, respectively

$$\mathrm{HA} + \mathrm{H_2O} = \mathrm{H_3O^+} + \mathrm{A^-}$$
$$\mathrm{DA} + \mathrm{D_2O} = \mathrm{D_3O^+} + \mathrm{A^-}$$

The isotope effect can be characterized by the ratio of the dissociation constants ($K_{\mathrm{H}} / K_{\mathrm{D}}$). For example, it was found experimentally that for OH-, NH-, SH- and CH-acids K_{D} is less than K_{H} ($K_{\mathrm{H}}/K_{\mathrm{D}} \approx 2.5$ to 3.9), i.e. the strength of these acids is less in $\mathrm{D_2O}$ than in $\mathrm{H_2O}$ and the weaker acids exhibit higher $K_{\mathrm{H}} / K_{\mathrm{D}}$ values.

For water and heavy water the values of the ionization constant at 25°C are 1.00×10^{-14} and 1.38×10^{-15}, which correspond to pH and pD values of 7.0 and 7.43, respectively. This has a practical consequence in the determination of pD values by glass electrodes: if the pH meter is calibrated by using buffer solutions prepared with $\mathrm{H_2O}$, then one must add 0.40 to the value shown by the instrument (‘pH meter reading’) in the case of a solution prepared with $\mathrm{D_2O}$ in order to obtain the value of pD (i.e. pD = pH meter reading + 0.40).

2.3.1. Isotope Exchange Equilibria

The ratio of the equilibrium constants K'_{A} and K_{A} [Eqs. (8) and (9)]

$$K = \frac{K'_{\mathrm{A}}}{K_{\mathrm{A}}} = \frac{[\mathrm{AX}][\mathrm{BX}']}{[\mathrm{AX}'][\mathrm{BX}]} \qquad (10)$$

gives the equilibrium constant of the isotope exchange reaction

$$\mathrm{AX}' + \mathrm{BX} = \mathrm{AX} + \mathrm{BX}' \qquad (11)$$

K indicates how the two isotopes are distributed between the two chemical compounds. Instead of K very often the elementary *separation factor* (*fractionation factor*) is used which is defined by

$$\alpha = \left(\frac{N}{N'}\right)_{\mathrm{AX}} \Big/ \left(\frac{N}{N'}\right)_{\mathrm{BX}} \qquad (12)$$

where N and N' are the atom fractions of the heavier and lighter isotopes in the compounds AX and BX. In general, α is defined in such a way that its value be larger than 1, i.e. the compound in which the heavier isotope is enriched is in the numerator of Eq. (12). It should be noted that α is only equal to K, if one atom in each molecule takes place in the isotope exchange. A separation factor of 1.050 is often referred to as a "5% isotope effect". Some examples for isotope exchange reactions (the values of K for 25°C are given in parenthesis):

$$\mathrm{H_2O + HD = HDO + H_2O} \quad (K = 3.35)$$
$$\mathrm{H_2O + HDS = HDO + H_2S} \quad (K = 2.26)$$
$$\mathrm{^{13}CO_2 + {}^{12}CO_3^{2-} = {}^{12}CO_2 + {}^{13}CO_3^{2-}} \ (K = 1.012)$$
$$\mathrm{H_2{}^{18}O + 1/3C^{16}O_3^{2-} = H_2{}^{16}O + 1/3C^{18}O_3^{2-}} \quad (K = 1.026)$$
$$\mathrm{^{15}NH_3 + {}^{14}NH_4^{+} = {}^{14}NH_3 + {}^{15}NH_4^{+}} \ (K = 1.035)$$

The largest isotope effects can be expected for deuterium (or tritium) – hydrogen isotope exchange reactions. However, isotope effects can also be readily detected in exchange reactions for other light elements. For example, the heavier carbon isotope ($^{13}\mathrm{C}$) enriches (~1%) in aqueous carbonate compared with gaseous carbon dioxide. In the equilibrium of ammonia gas with aqueous solutions of ammonium salts the $^{15}\mathrm{N}/^{14}\mathrm{N}$ ratio is 3.5% higher in solution than in the $\mathrm{NH_3}$ gas.

The equilibrium constants for isotope exchange reactions, similarly to those of ordinary chemical reactions, are functions of temperature. However, contrary to expectations that the magnitudes of the equilibrium constants decrease monotonically with increasing temperature, their temperature dependences may show striking 'anomalies', such as maxima, minima, inflections, single and multiple inversions ('cross-overs'). The temperature dependence of the separation factor constitutes the basis of the ‘dual temperature’ processes used for the production of heavy water. For example, in the water-hydrogen sulfide (Girdler-Sulfide) exchange process (Section 3.1), in the hot tower ($\alpha = 1.8$ at 130°C) deuterium passes from the liquid water to the gaseous hydrogen sulfide, whereas in the cold tower ($\alpha = 2.2$ at 30°C) the equilibrium of the exchange reaction shifts to the right, so in the net process deuterium passes from the gas to the liquid.

When stable isotopes are used for example as tracers for *in vivo* metabolic studies, typically the tracer flux is being measured and inferences are made about the flux of the material being traced (‘tracee’). When there is no isotope fractionation, the flux of the heavy tracer is equal to the flux of the lighter major isotope and hence the tracee flux. However, when there is isotope fractionation the fluxes of the heavy tracer and tracee are not equal and thus the flux derived from the kinetic analysis of the tracer is not equal to that of the tracee. For example, $^{18}\mathrm{O}$ is fractionated between water and carbon dioxide ($\alpha = 1.041$ at 25°C) thus the rate of removal of $^{18}\mathrm{O}$ by $\mathrm{CO_2}$ is 4.1% greater than the rate of $^{16}\mathrm{O}$ removal. Because $^{16}\mathrm{O}$ comprises 99.8% of the oxygen pool, the rate of $\mathrm{CO_2}$ production is essentially equal to the rate of $^{16}\mathrm{O}$ removal by $\mathrm{CO_2}$, which will be less by 4.1% than that measured from $^{18}\mathrm{O}$. Without taking this correction into account the calculated tracee flux will be in error. On the other hand, the isotope effect becomes negligible in the distribution of the isotopes of heavier elements; therefore no corrections are necessary in these tracer experiments.

The distribution of isotopes between isotopic molecules is a special case of isotope exchange reactions, e.g.

$$\mathrm{H_2O + D_2O = 2HDO}$$

It should be noted that the HDO molecules cannot be isolated from the liquid $\mathrm{H_2O\text{-}D_2O}$ mixture owing to the above reaction (which is fast). The question arises how the isotopes are distributed between the different isotopic molecules. By assuming random isotope distribution the mole fractions of the isotopic molecules $\mathrm{AX_2}$, $\mathrm{AXX'}$ and $\mathrm{AX'_2}$ are $(1-x)^2$, $2(1-x)x$ and x^2, respectively, where x is the atom fraction of the lighter isotope ($\mathrm{X'}$). This means, for example, that in natural water which contains about 0.015 atom percent D (abbreviated as 0.015 atom% D), practically all the deuterium atoms are in the form of HDO. In reality, however, isotope effects can be observed even in these reactions, thus for example the equilibrium constant for the above reaction is 3.75 at 25°C instead of 4 (which would correspond to the random distribution).

The equilibrium constants for isotope exchange reactions can be calculated by the statistical thermodynamic method used for the calculation of equilibrium constants of ordinary chemical reactions. However, the calculation becomes considerably easier in the case of isotope exchange reactions, since, within the framework of the Born–Oppenheimer approximation the zero of energy is the same for the isotopic molecules.

The equilibrium constant (K) for the isotope exchange reaction (11) can be written as

$$K = \frac{Q_{AX} Q_{BX'}}{Q_{AX'} Q_{BX}} = \left(\frac{Q}{Q'}\right)_{AX} \Big/ \left(\frac{Q}{Q'}\right)_{BX} \tag{13}$$

where Q is the partition function of the molecule. It can be seen that the equilibrium constant can be expressed through the ratio of the partition functions of isotopic molecules (Q/Q'). These have been calculated for many compounds and are available for different temperatures in the literature.

In the calculation of equilibrium constants and in the theory of isotope effects the so-called *reduced partition function ratio* (RPFR), introduced by Bigeleisen and Mayer in 1947, plays an important role. The RPFR (f) in the case of an ideal gas is given in the harmonic oscillator approximation (the internal vibrations of the molecule are treated as harmonic oscillators) by the expression

$$f = \prod_{i}^{3n-6} \frac{u_i}{u_i'} \left(\frac{1-\exp(-u_i')}{1-\exp(-u_i)}\right) \exp\left(\frac{u_i' - u_i}{2}\right) \tag{14}$$

where $u_i = hc\nu_i/(kT)$ (ν_i is the harmonic frequency – actually the wavenumber – of vibrational mode i in cm^{-1}), $3n\text{-}6$ is the number of vibrational modes (n is the number of atoms in the molecule). The equilibrium constant for the isotope exchange reaction (11) can be written in terms of the reduced partition function ratios as

$$K = \left(\frac{s_{AX'}}{s_{AX}}\right)\left(\frac{s_{BX}}{s_{BX'}}\right)\frac{f_{AX}}{f_{BX}} \tag{15}$$

where the s values are the symmetry numbers of the molecules. The ratio of the symmetry numbers corresponds to the random isotope distribution and to the equilibrium constant one would obtain by using classical statistical mechanics. For example, as the symmetry numbers for H_2O, D_2O and HDO are 2, 2 and 1, respectively, the symmetry number ratios in Eq. (15) give a value of 4. It is important to emphasize that the symmetry number factor leads to no fractionation of isotopes, the isotope effect is represented by the RPFRs, in other words, *any isotope separation by an isotopic exchange reaction must be a quantum effect.*

Equations (14) and (15) show that the equilibrium constants for isotope exchange reactions can be evaluated from the vibrational frequencies of the participating molecules. In terms of the RPFRs [Eq. (14)] some simple and practical relationships can be derived which help to understand the direction and magnitude of isotope fractionation between different molecules.

- At very high temperatures $(T \to \infty)$ $f = 1$.
- The value of the RPFR is nearly always larger than 1, since the vibrational

frequencies of the heavier isotopic molecule are mostly smaller than those of the lighter isotopic molecule, consequently $u_i < u_i'$.

- For pairs of isotopic molecules in which the substitution occurs at the same site by different isotopes of an element, f -1 is roughly proportional to the isotopic mass difference. For example, f -1 is twice as large for the molecule pair with $^{14}\mathrm{C}$ and $^{12}\mathrm{C}$ than for the molecule pair with $^{13}\mathrm{C}$ and $^{12}\mathrm{C}$, e.g. at 0°C

$$f\left(\frac{^{13}\mathrm{CO}_2}{^{12}\mathrm{CO}_2}\right)-1=0.2199\,,\quad f\left(\frac{^{14}\mathrm{CO}_2}{^{12}\mathrm{CO}_2}\right)-1=0.4469\,.$$

The following rule is also valid approximately: the larger the relative mass difference between the isotopes, the larger the isotope effect. For instance, H-D isotope effects are much larger than $^{235}\mathrm{U}$ - $^{238}\mathrm{U}$ isotope effects.

- The larger isotope molecule has a larger f value because it has more vibrational degrees of freedom, e.g. at 0°C

$$\left[f\left(\frac{(\mathrm{S}^{18}\mathrm{O}_3)^{2-}}{(\mathrm{S}^{16}\mathrm{O}_3)^{2-}}\right)\right]^{1/3}=1.080\,,\ \left[f\left(\frac{(\mathrm{S}^{18}\mathrm{O}_4)^{2-}}{(\mathrm{S}^{16}\mathrm{O}_4)^{2-}}\right)\right]^{1/4}=1.100\,.$$

- An atom with higher valency is characterized by a larger value of f, e.g. the values of f for the $^{34}\mathrm{S}/^{32}\mathrm{S}$ isotope effects (at 0°C) in the molecule SO_2, SO_3 and $(\mathrm{SO}_4)^{2-}$ are 1.053, 1.096 and 1.101, respectively.
- For pairs of molecules with multiple isotopic substitution (with the exception of D and T substitution) f is independent of the isotopic composition of the other atoms in the molecule, e.g. for carbon dioxide:

$$f\left(\frac{^{13}\mathrm{C}^{16}\mathrm{O}_2}{^{12}\mathrm{C}^{16}\mathrm{O}_2}\right)=f\left(\frac{^{13}\mathrm{C}^{18}\mathrm{O}_2}{^{12}\mathrm{C}^{18}\mathrm{O}_2}\right).$$

- A very useful rule of thumb is the following: the heavier isotope enriches in that isotopic molecule which has a larger f, in other words, *the heavier isotope accumulates where the binding is stronger*.

The value of the equilibrium constant for the isotope exchange reaction between real gases can be taken, to a good approximation, to be equal to that of ideal gases. For reactions taking place in the liquid phase, K can be obtained from its value in the gaseous phase and the vapor pressures of the isotopic compounds.

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Biographical Sketch

Gábor Jancsó was born in Budapest in 1941. He graduated with a degree in chemistry from Eötvös Loránd University (Budapest, Hungary) in 1964 and joined the Central Research Institute for Physics of the Hungarian Academy of Sciences. He is currently Scientific Advisor at the KFKI Atomic Energy Research Institute, Budapest and Honorary Professor of Chemistry at the Eötvös Loránd University. In 1969-1970 and 1976-1977 he spent one-year study leaves at the Chemistry Department of the University of Tennessee. From 1982 to 1984 he was a visiting scientist at the Max Planck Institut für Chemie. His research interests include the investigation of the effects of isotopic substitution on the properties of liquids and mixtures, molecular dynamic simulation of liquid water and aqueous solutions and the structural and dynamic properties of aqueous solutions using neutron diffraction.