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Chemistry of Isotopes

Isotope chemistry has opened new areas of chemical physics, geochemistry, and molecular biology.

Jacob Bigeleisen

Isotopes were discovered on the basis of differences in nuclear properties but identity of chemical properties. Nevertheless, Fajans recognized at an early date that properties of matter which depend on the frequencies of atomic and molecular vibrations would be different for the isotopes of a given substance. Isotope effects can also arise from other properties of atoms and molecules. As judged by the usual standards of chemistry, isotope effects are small. They can be measured accurately by modern physical methods and are subject to detailed theoretical interpretation. For these reasons the chemistry of isotopes is of interest per se. Isotope effects have useful applications in both pure and applied science. In applied science the obvious application is to isotope separation. In pure science the differences in physical and chemical properties of isotopes can be used to study such diverse problems as molecular structure, quantum effects, and chemical kinetics in the field of chemical physics; paleotemperature and biogenesis in geochemical studies; and the growth and morphology of plants and animals in the biochemical and medical sciences. This article gives a brief introduction to the principles of isotope chemistry and some selected examples from the application of isotope effects to problems in pure science.

What is meant by "isotope effects" or the "chemistry of isotopes" can be illustrated by three experiments with water. Natural water is a mixture of light and heavy water. If ordinary water is equilibrated with hydrogen gas, say by means of a platinum catalyst, then at equilibrium the ratio of deuterium (heavy hydrogen) atoms to protium (light hydrogen) atoms in the water is found to be 3.7 times the ratio of deuterium to protium atoms in the hydrogen gas. This ratio, 3.7, is found if the equilibration is carried out at room temperature, and it becomes progressively smaller, approaching unity, as the equilibration temperature is increased. The deuterium atoms behave differently from the protium atoms in these two compounds, water and hydrogen. This is ordinary chemistry. If water is electrolyzed, hydrogen appears at the cathode and oxygen at the anode. Comparison of the deuterium-to-protium ratio in the water being electrolyzed with that in the evolved hydrogen shows the water to be richer in deuterium by a factor of 3.7 to 9. The precise difference depends on the electrode materials and the conditions of electrolysis. Finally, if the deuterium abundance in liquid water is compared with that in vapor in equilibrium with the liquid, the liquid is again found to be richer in deuterium, but this time by a factor of only 1.07. The discrimination between deuterium and protium in water depends on the process involved.

In classical theory there are no differences in the physical or chemical processes of systems at equilibrium. In processes which depend on the velocities of particles, protium may react more rapidly than deuterium by a factor of $2^{\frac{1}{2}}$. This is a consequence of the kinetic theory which states that the kinetic energy, $\frac{1}{2}\, mv^2$, is proportional to the absolute temperature. Thus, at a given temperature the velocity v is proportional to $(1/m)^{\frac{1}{2}}$ (where m is mass), or $v_{\mathrm{H}} = 2^{\frac{1}{2}} v_{\mathrm{D}}$. The classical theory is seen to be inadequate to explain the observed differences in chemical properties of protium and deuterium both in systems which are at equilibrium and in processes which depend on particle velocities. One must, therefore, turn to the quantum theory to look for an explanation of the observed phenomena. In fact, it is just for this reason that isotope effects are so useful in the study of quantum effects in chemistry.

Basis of Chemical Isotope Effects

The energy of a molecule or a collection of molecules is described in terms of the electronic energy plus the translation, rotation, and vibration of the molecules. To this must be added the energies associated with the mutual interactions of these motions. For all gases, translation and rotation at room temperature are adequately described by classical mechanics. Anything which is describable in terms of classical mechanics contributes nothing toward differences, at equilibrium, in the chemical properties of isotopes. From observations of atomic and molecular spectra it is concluded that the differences in the electronic energies of protium and deuterium in their various compounds cannot result in an effect greater than 0.5 percent. This leaves, as the sole potential large origin of "isotope effects," the molecular vibrations.

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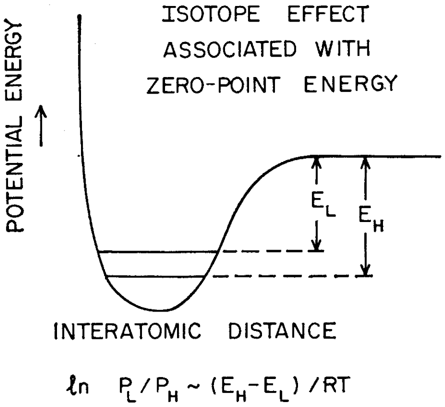
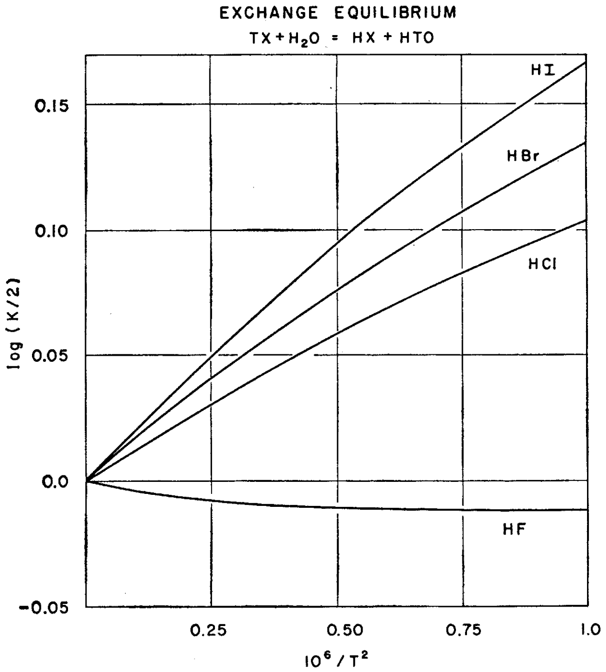


Fig. 1. Schematic potential-energy curve for the interaction of two atoms in a stable molecule or between two molecules in a liquid or solid.

Figure 1 shows schematically the energy of a diatomic molecule as a function of the distance between the two atoms. When the atoms are far apart, they move independently of one another. As they approach one another there is an attractive force. If the atoms get closer to one another than the distance corresponding to the diameter of the stable molecule, they repel one another and the energy increases rapidly. Another way of looking at this repulsion is to observe, simply, that the atoms have finite size and that both cannot occupy the same place without one or both of them being squeezed. This compression takes work. According to the quantum theory the molecule cannot assume any energy on the continuous curve shown in Fig. 1. It is restricted to certain discrete energy levels. The lowest level is not at the minimum of the energy curve but is above it by an amount $\frac{1}{2}hv$, where h is Planck's constant and v is the frequency with which the atoms in the molecule vibrate with respect to one another. The vibrational frequency of a molecule depends inversely on the masses of the atoms in the molecule. It also depends directly on the forces holding the atoms together in the molecule. The forces in a molecule depend on the electron arrangements, the nuclear charges, and the positions of the atoms in the molecule. For our purposes it suffices to consider these forces identical for isotopes of a given substance. However, since isotopes differ in mass, two molecules with the same chemical formula but of different isotopic species—for example, H_2 and D_2—will have different vibrational frequencies. They will have different zero-point energies; the molecule of the heavy isotope will have a lower zero-point energy than the molecule of the light isotope. This is shown schematically in Fig. 1, where the upper horizontal line represents the zero-point energy of the light molecule and the lower line that of the heavy one.

Now let us consider the energy necessary to dissociate the diatomic molecule when all the molecules are in the ground vibrational state. This energy is E_L for the light molecule but E_H for the heavy molecule. There is a difference in the energy necessary to dissociate the two kinds of isotopic molecules. Associated with the difference in dissociation energies of isotopic molecules there is a corresponding entropy difference. The entropy change serves to make the difference in free energies, or chemical potentials, of isotopic molecules smaller than the energy differences of the molecules. Later I show that the entropy difference is smaller than the energy difference, and that thus the free-energy difference of a pair of isotopic molecules behaves qualitatively similarly to the zero-point energy difference. The absolute entropies of a pair of isotopic molecules differ if one member of the pair is less symmetrical than the other. This a priori difference in the probabilities that symmetrical systems will form, as opposed to asymmetrical systems, does not lead to a difference in chemical properties of isotopes. A qualitative discussion of isotope effects can therefore be carried out by considering zero-point energies.

First, consider the chemical reaction in which radioactive bromine atoms (Br^*) exchange positions with ordinary bromine atoms (Br) between two chemical species. The species to be discussed are lithium bromide dissolved in water and benzyl bromide dissolved in ethylene diacetate (abbreviated organic,



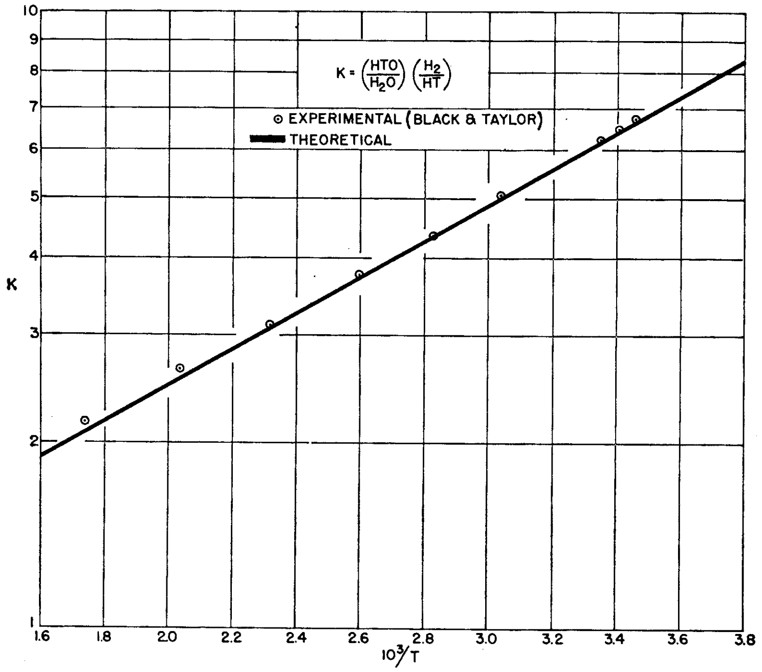


Fig. 2 (left). Fractionation of tritium and protium between the hydrogen halides and water at temperatures above 1000°K. Fig. 3 (right). Experimental and calculated equilibrium constants for the exchange reaction $HT + H_2O = HTO + H_2$.

Table 1. Protium-deuterium fractionation factors for various compounds compared with water at 25°C. [Fractionation factor is defined as $(D/H)_{\text{compound}}/(D/H)_{\text{water}}$.]

Compound	Fractionation factor
O-H bonds	
Acetic acid	1.03
Methanol	1.0
Ethanol	1.11
n-Amyl alcohol	1.09
Benzyl alcohol	1.10
Phenol	1.07
N-H bonds	
Ammonia	0.954
Formamide	1.04
Acetamide	1.02
Aniline	1.11
C-H bonds	
Benzene	0.87
Naphthalene	.87
Toluene (all)	.9
Acetone	.85
Pentene	.85
Cyclohexane	.88
S-H bonds	
H_2S	.455
Ethyl SH	.43
i-C_3H_7SH	.495
n-C_3H_7SH	.493

or org). The ethylene diacetate and water are sparingly soluble in one another. The lithium bromide is sparingly soluble in the organic, and the benzyl bromide is sparingly soluble in water. If initially all the radioactivity is in the lithium bromide and none is in the benzyl bromide, the radioactivity will increase in the benzyl bromide and decrease in the lithium bromide (*1*). These results can be summarized by the equation

$$\phi CH_2Br(org) + Br^{*-}(H_2O) = \phi CH_2Br^*(org) + Br^-(H_2O)$$

At equilibrium, when the radioactivity in the benzyl bromide does not increase with time and the activity of the bromide dissolved in water does not decrease, the following relationship is found between the concentrations of the different molecular species:

$$\frac{(\phi CH_2Br^*)(Br^-)}{(\phi CH_2Br)(Br^{*-})} = \frac{\phi CH_2Br^*/\phi CH_2Br}{Br^{*-}/Br^-} = K$$

$$K = \frac{(Br^*/Br)_{\text{org}}}{(Br^*/Br)_{H_2O}} = 1.00$$

The specific activities of the water and organic phases are equal at equilibrium. The radioactive bromine acts as a random tracer. The random distribution results from the fact that the differences in zero-point energies of the various bromine isotopes are small with respect to the differences in their thermal energies. The vibrations of the molecules in which the bromine atoms participate behave sufficiently close to classical mechanics that there is no discrimination between isotopes.

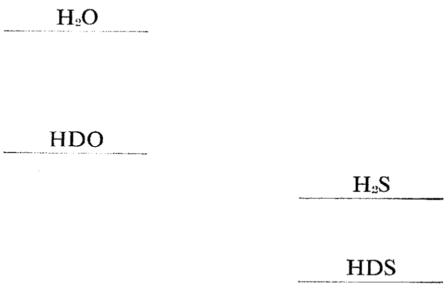
Now consider the isotopic exchange reactions involving protium and deuterium, between liquid water and hydrogen sulfide gas:

$$H_2O_{(l)} + HDS_{(g)} = HDO_{(l)} + H_2S_{(g)}$$

The chemical binding of hydrogen to oxygen is much stronger than that of hydrogen to sulfur. The H_2O and H_2S molecules have similar structures. Each molecule has three vibrational frequencies, and there is a one-to-one correspondence of the types of vibrations in the two molecules. The important difference is that each vibration in the water molecule has a higher frequency than that in the hydrogen sulfide molecule. For such a molecule the zero-point energy, E^0, is

$$E^0 = \sum_{i=1}^{3} \frac{1}{2} h\nu_i$$

The relative zero-point energies can be depicted by the following scheme,



The zero-point energies increase sequentially from HDS, H_2S, HDO, to H_2O.

The energy change in the chemical reaction is

$$\Delta E = E^0(H_2S) + E^0(HDO) - E^0(HDS) - E^0(H_2O)$$

$$\Delta E = [E^0(H_2S) - E^0(HDS)] - [E^0(H_2O) - E^0(HDO)]$$

The relationship of the relative concentrations of different molecules at equilibrium is

$$K = \frac{(HDO)/(H_2O)}{(HDS)/(H_2S)} = \frac{(D/H)_{H_2O}}{(D/H)_{H_2S}} = 2.35$$

at 25°C.

$$\ln K \approx -\Delta E/RT$$

where R is the gas constant.

$$\ln K \approx \frac{[E^0(H_2O) - E^0(HDO)]}{RT} - \frac{[E^0(H_2S) - E^0(HDS)]}{RT}$$

The deuterium atoms concentrate preferentially in the water (*2*). *The heavy isotope goes preferentially to the chemical compound in which the element is bound most strongly*. This rule has been shown to hold when the energy change for the exchange reaction can be calculated by assuming all the molecules to be in the lowest vibrational energy state and the entropy change to be negligible.

We now inquire about what happens to the isotope distribution when the molecules get distributed among the higher vibrational states. At very high temperatures the rule is definitely that the heavy isotope prefers the chemical species in which the element has the strongest binding. This will generally, but not necessarily, be the behavior over the entire temperature range. In some special cases deviations from this rule will occur. These are matters of interest for the expert. Figure 2 shows the equilibrium constants for the exchange of tritium and protium between the hydrogen halides and water above 1000°K. The isotope fractionation faithfully reproduces the chemical affinity of the halogens F > Cl > Br > I. The tritium favors the HF most and the HI least. The isotope distribution rule is valid at high temperatures, where the higher vibrational states become appreciably populated. In fact, it can be shown through the methods of statistical mechanics that this high-temperature behavior is the fundamental rule (*3*).

The quantitative treatment of isotopic exchange equilibria is not much more complicated than the zero-point energy approximation. For the isotopes of all elements other than hydrogen, the zero-point energy factor ½ is to be replaced by a function of the vibrational frequencies $G(u)$ such that

$$G(u) = \frac{1}{2} - \frac{1}{u} + \frac{1}{e^u - 1}$$

where $u = h\nu/kT$. The quantities h and k are, respectively, Planck's and Boltzmann's constants. At low temperatures or large u, $G(u)$ approaches the zero-point energy value of ½ asymptotically. At high temperatures $G(u)$ goes to zero and the equilibrium differences in chemical properties of isotopes vanish. Some mathematical approximations in the derivation make the $G(u)$ function not applicable to the isotopes of hydrogen. Nevertheless, the same principles hold. The hydrogen isotope effect at

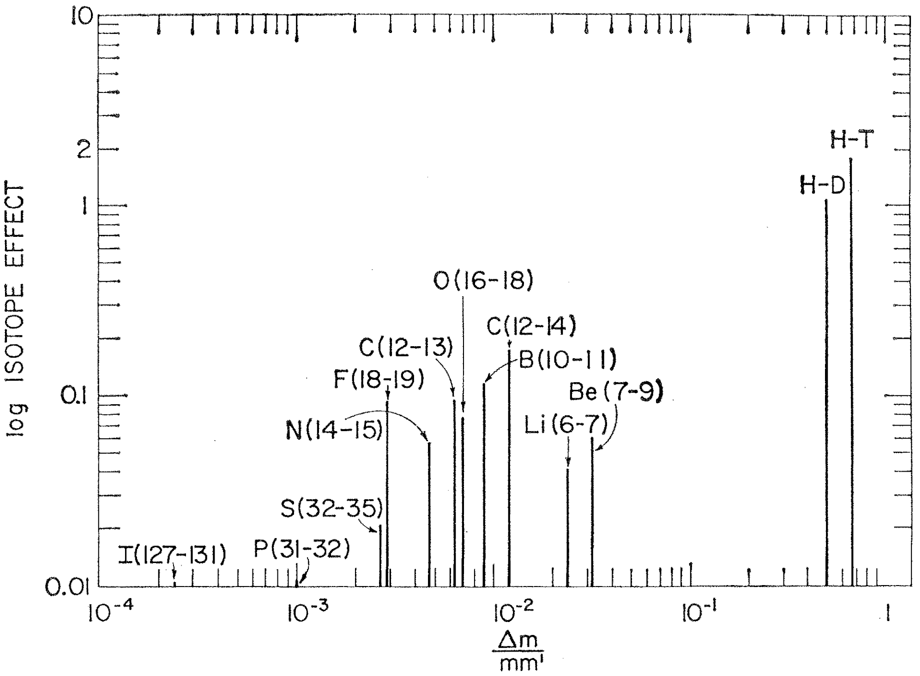


Fig. 4. Maximum isotope effects for elements in the first half of the periodic table. (Values in parentheses are atomic weights.)

room temperature is primarily a function of the type of chemical bond. Table 1 lists the protium-deuterium equilibrium fractionation factors for a variety of compounds relative to water at 25°C. It is clear that compounds with similar types of bonds have similar fractionation factors or isotope effects. To get appreciable isotope effects one has to compare chemical compounds that have significant differences in chemical bonding. The largest effects are to be observed when the isotopes in a compound with strong chemical bonding are compared with the free monatomic element, which has no bonding. (The function of Bigeleisen and Mayer shows that the free element is a logical basis from which to make comparisons of isotope effects.)

Quantitative Aspects of Isotope Effects

It is important to demonstrate the degree to which our ideas about the origin of equilibrium isotope effects agree with experiment. For this purpose detailed knowledge is required of the vibrational frequencies of polyatomic molecules and their change with isotopic substitution. Some of this information can be obtained from spectroscopic measurements; some depends on calculations based on well-established principles of mechanics (*4*). For the isotopes of hydrogen, the theory of small vibrations is not adequate, and the large amplitudes (0.1Å) of the vibrations associated with small masses complicate the analysis of the energy levels. The analysis of the spectra of the H_2 and H_2O molecules have reached a high degree of refinement. The equilibrium constants for the reaction

$$HT + H_2O = HTO + H_2$$

calculated from the spectra without any arbitrary or adjustable constants are shown as the solid line in Fig. 3. The circles are the experimental data obtained some 20 years ago by J. F. Black and H. S. Taylor (*5*) in the temperature range 15° to 300°C. The calculations are in satisfactory agreement with experiment. Table 2 gives a comparison of experimental and theoretical equilibrium constants for some typical isotope exchange reactions of the light elements.

The theory of equilibrium isotope effects for gaseous molecules has now reached a rather advanced stage of development. Theorems and corollaries have been derived which relate the isotope effect directly to the structure and chemical bonding in the molecule. For complex molecules, procedures are now available for direct computation by means of high-speed digital computers (*6*). The necessary input data are the structure and forces in the molecule. Conversely, experimentally determined isotope effects can be used to evaluate such quantities.

Questions naturally arise about how large isotope effects can get, and how they depend on the mass of the element and its chemistry. Theory can provide unequivocal answers to these questions. The logarithm of the chemical isotope effect in a given compound is proportional to the mass difference (Δm) of the isotopes, divided by the product of the masses of the isotopic atoms (this product is a characteristic constant for the isotopes of a given element), multiplied by the force constant acting to restore the isotopic atom when it is displaced from its equilibrium position in the molecule. The force constant is a measure of the strength of the chemical binding. Mathematically, the relationship is expressed as

$$\log(\text{isotope effect}) \sim (\Delta m/mm') \cdot \text{force constant}.$$

The maximum isotope effect between two compounds occurs when the force constant in one of them is zero. This compound is the free gaseous atom. A histogram of maximum isotope effects for elements in the first half of the periodic table is given in Fig. 4. A number of features are noteworthy. The effects range from a factor of near 100 for protium-tritium to 1 percent for the isotopes of phosphorus and iodine. Some salient chemical facts manifest themselves if one considers the effects in sulfur, nitrogen, oxygen, carbon, and fluorine. The strengths of the

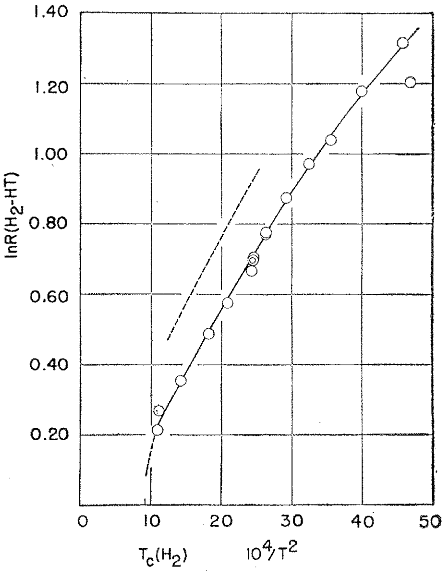


Fig. 5. Distribution coefficient for HT, in solution in H_2, between liquid and vapor as a function of temperature. Dotted curve is that calculated for a solution of D_2 in H_2. [From Bigeleisen and Kerr (*8*), courtesy *J. Chem. Phys.*]

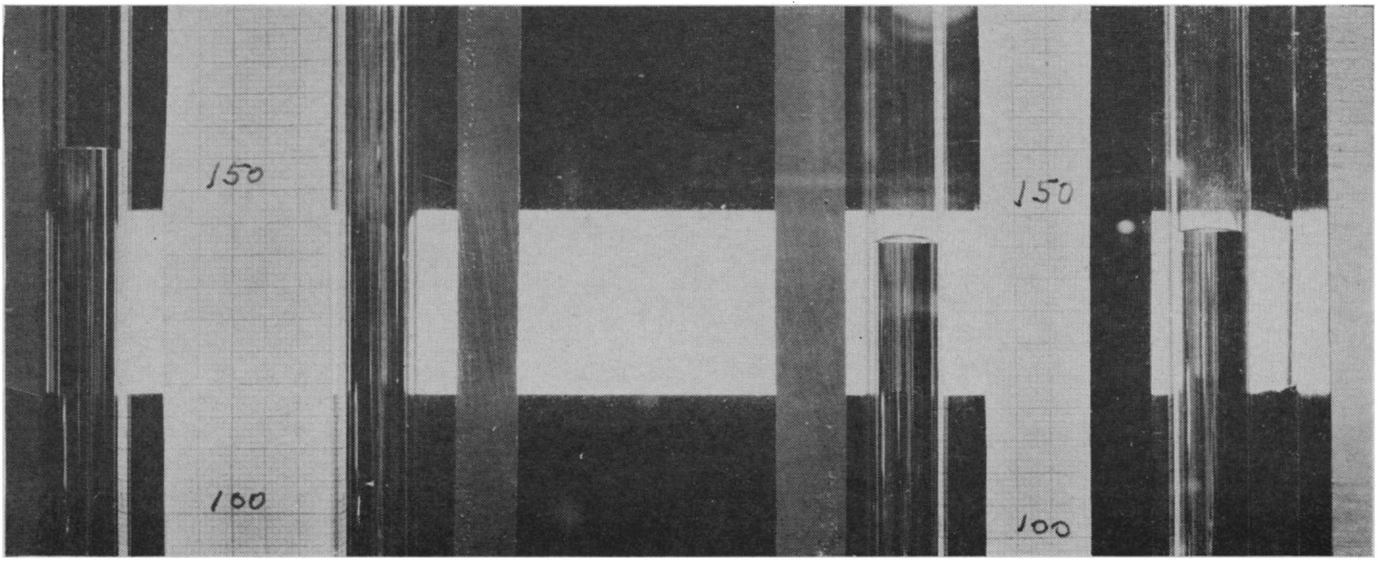
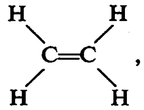
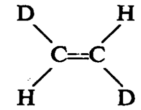
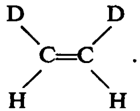
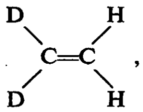


Fig. 6. The three mercury levels shown measure the vapor pressures of (left to right) ordinary ethylene , *trans*-ethylene-1,2-d_2, , and *cis*-ethylene-1,2-d_2, . (The *gem*-ethylene-1,2-d_2, , is very similar to the *cis*-form and is not shown in the photograph.) Note that the *trans*- form is the most volatile.

chemical bonds are in the order in which the elements are listed in the preceding sentence, and these bond strengths dominate the features of the isotope effects for these elements, all of which have comparable values of $\Delta m/mm'$.

This brief exposition of the principles of isotope chemistry can serve as a background for the discussion of applications of isotope effects in chemical physics, geochemistry, and biology. The choice of examples is representative of some of the types of problems which have been attacked. A significant omission is the big field of chemical kinetics. To do justice to the impact that the study of isotope effects has had on such topics as transition-state theory, potential-energy surfaces for chemical reactions, tunneling in chemical reactions, bonding changes of neighboring groups in the transition state (secondary isotope effects), and definitive evidence on reaction mechanisms would require a separate article.

The subject of isotope effects in the interaction of molecules with one another is one in which major progress has been made in the last few years. A number of new phenomena have been discovered through use of this unique tool, and I should like to review some of the results. The experiments consist of measurement of the vapor pressures of pure isotopic compounds or, alternatively, the equilibrium fractionation of an isotopic mixture between two phases—for example, vapor and liquid. I exclude from the discussion the behavior of the isotopes of helium, which, although fascinating, constitutes a subject in its own right.

The simplest systems are, naturally, the monatomic rare gases. In the liquid or solid phase there is a zero-point energy associated with the intermolecular potential. In the dilute vapor the interaction is negligible (or can be corrected for). From Fig. 1 we can see that the light isotope has the higher vapor pressure. The theory of this effect was first developed by Lord Cherwell (F. A. Lindemann) in 1919. Yet a quantitative understanding of the phenomenon has been arrived at only within the past 5 years. Part of the difficulty is the high precision necessary for obtaining the experimental data. Reliable data now exist for the isotopes of neon and argon, from independent measurements of different types (*7*). The data provide new information concerning intermolecular forces. They give information concerning the range and strength of the intermolecular force and its curvature at the minimum of the potential curve. The values for the curvature differ from those obtained from heat capacity measurements (Θ_D). The discrepancies are real and have provided information about the deviation of the potential at the minimum from a simple parabola. Such information could not be easily obtained from thermal measurements alone.

There is a sharp discontinuity in the isotope effect on the vapor pressure at the melting point. For neon this results from a reduction in the coordina-

Table 2. Comparison of experimental (K_{exp}) and theoretical (K_{calc}) equilibrium constants for isotope exchange reactions. [From the compilation by Urey (*15*)]

Reaction	T (deg K)	K_{exp}	K_{calc}
$H_2 + DI = D_2 + HI$	600	1.21±0.02	1.207
$HT + H_2O = H_2 + HTO$	298	6.26±0.1	6.35
$1/2\ C^{16}O_2 + H_2{}^{18}O(liq) = 1/2\ C^{18}O_2 + H_2{}^{16}O(liq)$	273	1.046	1.044
$^{15}NH_3 + {}^{14}NH_4{}^+ = {}^{14}NH_3 + {}^{15}NH_4{}^+$	298	1.034	1.035
$H\,^{12}CN + {}^{13}CN^- = H\,^{13}CN + {}^{12}CN^-$	295	1.026	1.030
$^{12}CO_3{}^{--} + {}^{13}CO_2 = {}^{13}CO_3{}^{--} + {}^{12}CO_2$	273	1.017	1.016
$1/3\ C^{16}O_3{}^{--} + H_2{}^{18}O = 1/3\ C^{18}O_3{}^{--} + H_2{}^{16}O$	273	1.036	1.033

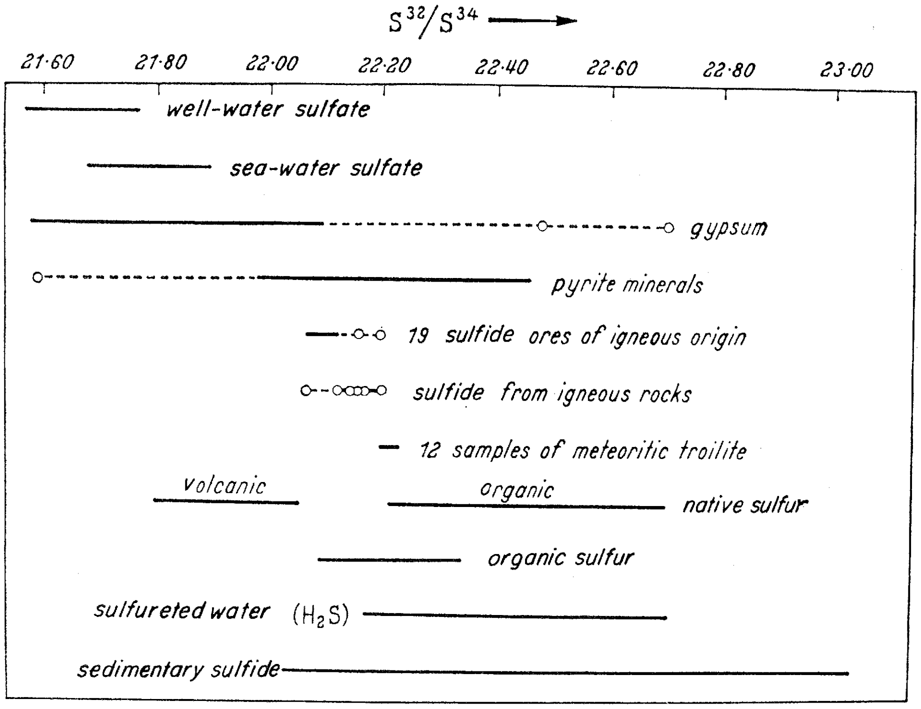
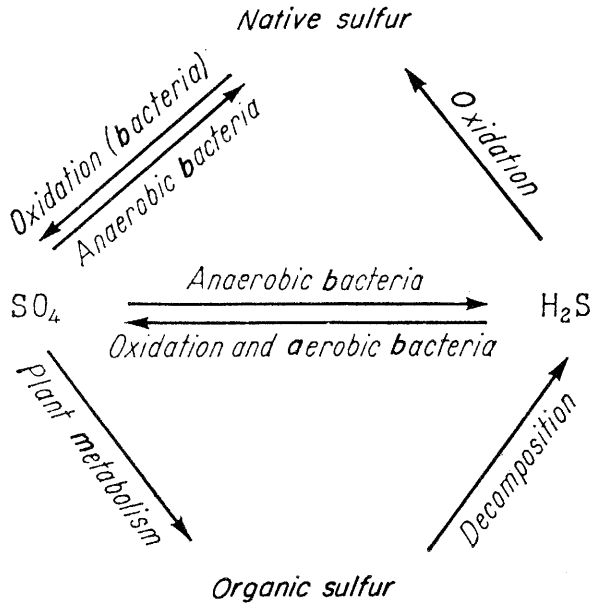


Fig. 7. Isotope distribution of terrestrial and meteoritic sulfur. [From Thode *et al.* (*14*), courtesy *Geochim. Cosmochim. Acta*]

tion number in the solid, 12, to 8.8 in the liquid. The nearest-neighbor distance and the atom-pair interaction are unchanged in the liquid from the distance and interaction in the solid at the melting point.

The behavior of polyatomic molecules is more complicated. In some cases, particularly in comparisons of deuterocarbons with hydrocarbons, the heavy isotope has been found to have the higher vapor pressure. Even equivalent isomers of isotopic molecules show different behavior. These phenomena, as well as others, led to the development of a more general theory than Lord Cherwell's, and from this more general theory a number of new phenomena have been predicted. Experiments have confirmed these predictions and have led to the discovery of a number of new phenomena connected with rotation in liquids and solids. These in turn have led to further amplification of the theory. When two molecules interact with one another, not only is the motion of the molecule through space different from that of the free molecule but also the rotation of the molecule and the vibrations of the molecule are affected. Further, each of these motions becomes coupled to the other types of motions. A striking example of this is shown in Fig. 5, which gives experimental data on the fractionation of HT, in a dilute solution in H_2, between liquid and vapor. At temperatures between 20° and 28°K the HT molecule is 22 to 24 percent more volatile than the D_2 molecule, which has the same molecular weight. The difference in volatility between HT and D_2 arises from the fact that the center of gravity of the HT molecule is displaced from the geometric center of the molecule. This leads to a coupling of the translation and rotation in this molecule which is lacking in D_2. This is a new type of quantum effect discovered by means of isotope effects (*8*). The theory of the effect has been



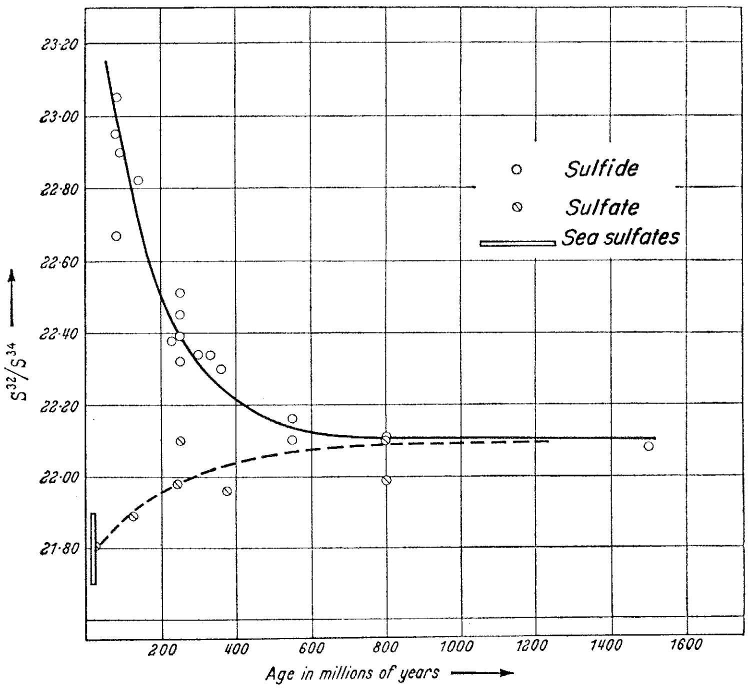


Fig. 8 (left). Sulfur cycle in nature. [From Thode *et al.* (*14*), courtesy *Geochim. Cosmochim. Acta*] Fig. 9 (right). The distribution of ^{34}S in sedimentary sulfides and sulfates of different ages. [From Thode *et al.* (*14*), courtesy *Geochim. Cosmochim. Acta*] developed (*9*) and is in good agreement with experiment.

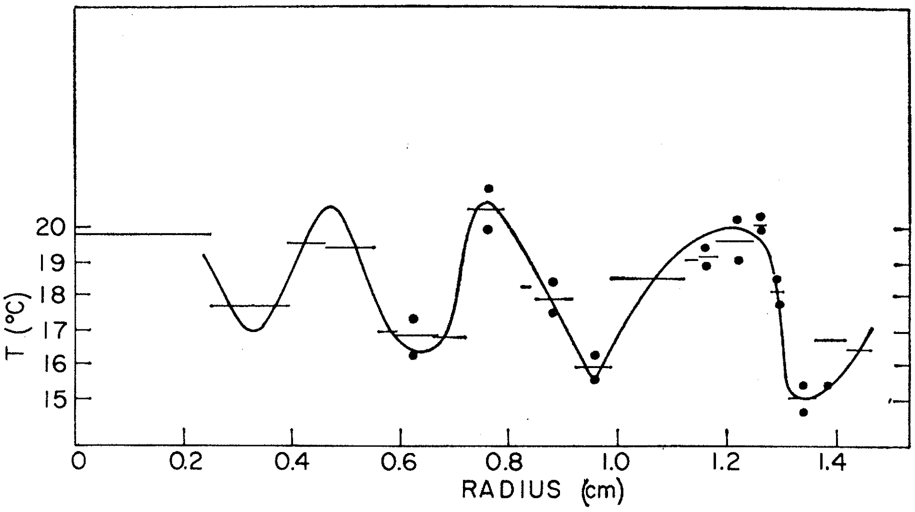


Fig. 10. Temperature at time of formation of a Jurrasic belemnite as a function of radius from the center of growth. [From Urey *et al.* (*16*), courtesy *Bull. Geol. Soc. Amer.*]

A simpler type of rotational effect was demonstrated for nitrous oxide. This molecule is linear, with the structure NNO. The sequence of the isotopic species with respect to vapor pressure has been found to be $^{14}N^{14}N^{16}O > {}^{14}N^{15}N^{16}O > {}^{15}N^{14}N^{16}O > {}^{14}N^{14}N^{18}O$. The difference in vapor pressure between the two species containing ^{15}N arises from hindered rotation of the molecule in the liquid.

A third type of rotational effect was discovered in the study of the vapor pressures of the deuterated ethylenes (*10*). Figure 6 illustrates the difference between the vapor pressures of *trans*- and *cis*-dideuteroethylene. This difference is in part due to hindered rotation, just as in the case of N_2O, but is principally due to the coupling of the rotation of the molecule about the C=C axis with the out-of-plane bending of the molecule in the liquid. These couplings are different for the different ethylenes because of symmetry considerations (*10, 11*).

Applications to Geochemistry

Some 25 to 30 years ago both Dole (*12*) and Nier (*13*) showed that the isotopic abundances of the light elements are not constant in nature. Since that time a branch of science, isotope geology, has matured which applies these variations to the investigation of geochemical and geological processes.

The first systematic studies of the variation in the abundances of sulfur isotopes in nature were carried out by Thode and his co-workers (*14*). A summary of their findings, which have since been confirmed and extended by others, is shown in Fig. 7. Several patterns emerge from the analyses. First, the heavy isotope ^{34}S is more abundant in sulfates than in native sulfur or sedimentary sulfides. The spread of sulfur-isotope abundances in meteoritic samples is small, and, further, such samples are almost identical with high-temperature ores. The average composition of all terrestrial samples, weighted in accordance with their relative natural abundances, is close to that of meteoritic and igneous sulfur. These results indicate that meteoritic and igneous sulfur have isotope abundances close to those of their primordial composition. The other terrestrial sources have been fractionated by means of chemical and physical processes. High-temperature processes show little, if any, isotope discrimination. This explains the close similarity of igneous terrestrial sulfides and meteoritic sulfur. The observed terrestrial fractionation agrees with the theory of isotope effects. The heavy isotope ^{34}S concentrates in the chemical species with the strongest chemical binding—namely, sulfate—and is depleted where the binding is weakest—in elemental sulfur, sedimentary sulfides, and hydrogen sulfide. More detailed calculations support these qualitative arguments.

Sulfur is turned over in nature in accordance with the cycle shown in Fig. 8. Note that cyclic, natural processes exist for the interconversion of sulfur among the various different chemical species. Over a long time scale the various species will reach isotope exchange equilibrium. The extent to which bacteria are involved in establishing the cycles is noteworthy. In another set of experiments Thode and his co-workers (*14*) measured the $^{32}S/^{34}S$ ratios in dated specimens of sedimentary sulfides and sulfates incorporated into limestones. Their findings are shown in Fig. 9. We note that samples older than 800 million years show no differences between sulfate and sulfide. Their $^{32}S/^{34}S$ ratio, 22.1, is identical with that of igneous sulfides and meteoritic sulfur. Recent samples show ^{34}S concentration in sulfate and ^{32}S concentration in sulfide. These results strongly suggest a time scale of the order of magnitude of 800 million years for the onset of the turnover of natural sulfur by the biological cycle.

Early in 1947 Urey (*15*) predicted that the temperature coefficient of the oxygen-isotope exchange equilibrium between carbonate and water might serve as a thermometer. Calculations and experiments showed (see Table 2) the $^{18}O/^{16}O$ ratio in carbonates to be some 3 percent larger than the ratio in liquid water. The temperature coefficient of this isotope exchange equilibrium was calculated to be 1.8×10^{-4} per degree Celsius. If carbonates exchange oxygen with water and if the equilibrium is "frozen in," then a determination of the isotope ratio with a precision of 0.2 per mil, or an absolute variation for the rare isotope ^{18}O by 1 part in 2.5 million, corresponds to a temperature difference of 1 °C. Such a determination was the goal that Urey and his associates set for

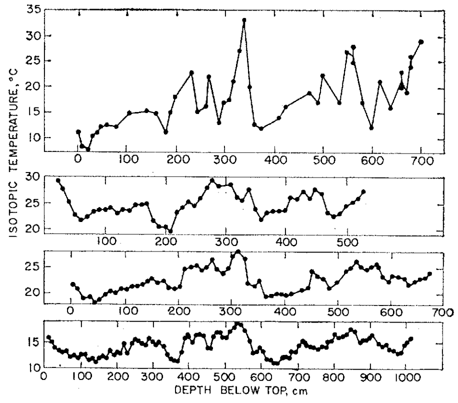


Fig. 11. Analyses of cores from (top to bottom) the Mediterranean, the Caribbean, the equatorial Atlantic, and the North Atlantic. (Scales are adjusted to correspond to equal geological times.) [From Emiliani (*17*), courtesy *Sci. Amer.*]

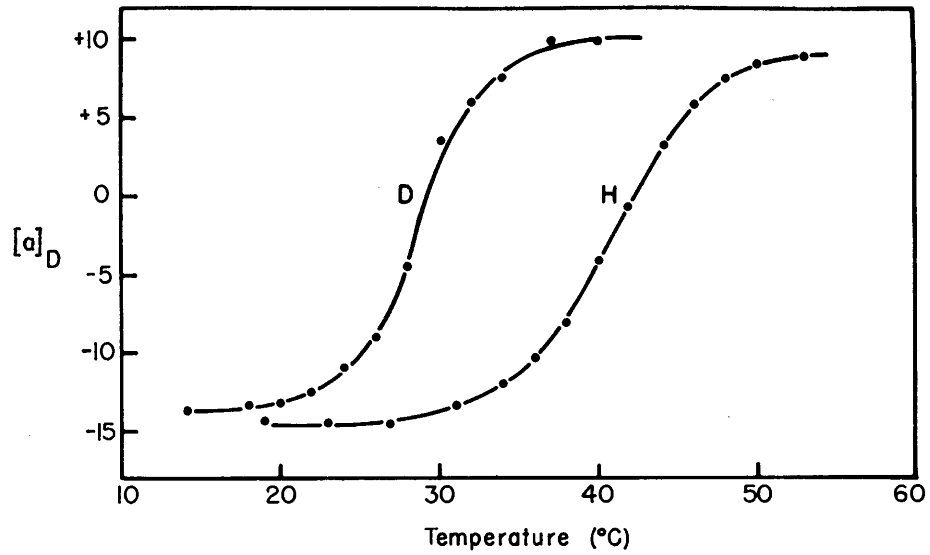


Fig. 12. Shift in transition temperature between deuterated and ordinary polybenzyl glutamate. $[\alpha]_D$ is specific optical rotation measured with the D line of sodium. [From Calvin *et al.* (*18*), courtesy *J. Amer. Chem. Soc.*]

themselves. Samples of $CaCO_3$ precipitated from solution fully confirmed these predictions concerning the magnitude and the temperature coefficient of the enrichment factor.

Figures 10 and 11 show some geochemical applications that have been made of the ^{18}O paleotemperature method. In one of the first tests of the method Urey and his co-workers (*16*) analyzed a Jurassic belemnite from the Isle of Skye. These extinct fossils are 150 million years old and have a backbone of pure calcium carbonate. Upon sectioning they show growth rings analogous to tree rings. In one such belemnite, 2.5 centimeters in diameter, 24 rings were analyzed, and the results were plotted as a function of the distance from the center. The mean temperature was measured to be 17.6°C. The seasonal variation is clearly indicated in Fig. 10 (*16*), which shows a life cycle of four winters and three summers, with a maximum temperature variation of 6°C. The belemnite certainly retained the temperature record. Emiliani (*17*) has found fossils of the tiny one-celled marine animals foraminifera particularly useful as samples. From them he has made ocean-temperature measurements covering the last 200,000 years (Fig. 11). The temperature variations are similar for the different oceans, but they differ in magnitude. The largest variations are found for the closed body of water, the Mediterranean. The absolute temperature differences between the oceans need no further explanation. Emiliani has measured the variations of ocean temperatures that occurred during the Pleistocene and has compared his results with solar radiation fluctuations calculated by Milankovitch. In his calculations Milankovitch considered the change in the summer and winter solar radiation at a given latitude which is due to perturbations in the earth's orbit. Some schools of geochemists correlate these perturbations with the periods of the glaciers during the Pleistocene. The evidence that glaciation is due solely to astronomical perturbations is not conclusive.

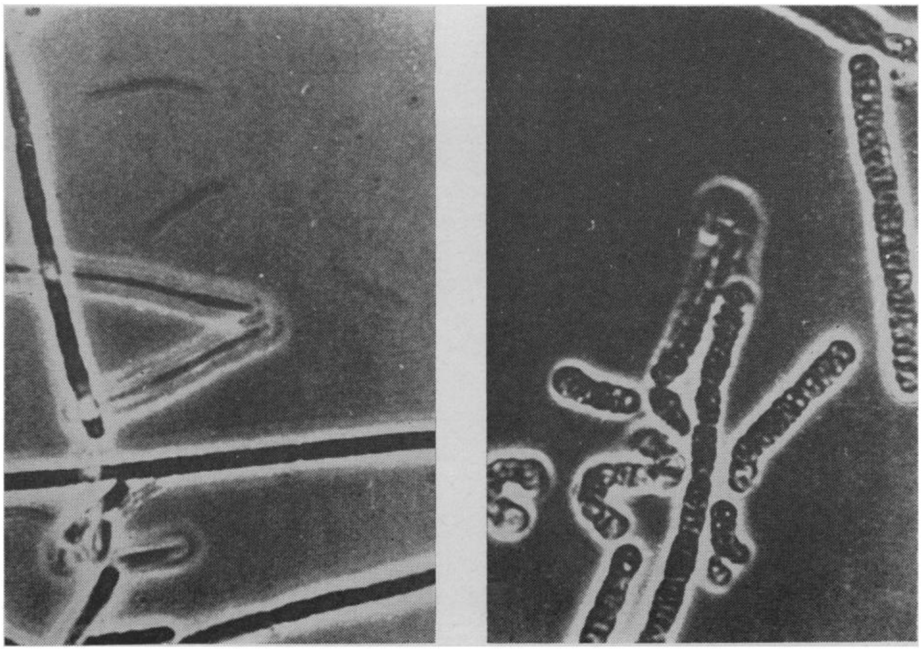


Fig. 13. Phase-contrast photomicrographs of blue-green algae grown in (left) H_2O and (right) D_2O. [From Crespi *et al.* (*19*), courtesy *Ann. N.Y. Acad. Sci.*]

Biological Effects of Deuterium

Shortly after the discovery of deuterium it was recognized, both by Urey and by G. N. Lewis, that the chemical and physical properties of protium and deuterium would be sufficiently different from one another to lead to marked differences in the biological activities of these isotopes. These predictions have now been fully verified, and biological studies of deuterated systems have become established as an important new tool in molecular biology. The field can be said to be in its infancy.

A model experiment was performed recently by Calvin, Hermans, and Scheraga (*18*). These authors studied the effect of deuteration on the transition from the helical to the random-coil structure in polypeptides, proteins, and enzymes. These transformations, which are of fundamental biological importance, involve the formation and rupture of hydrogen bonds from one amino acid group in the molecule to another. If the strength of the hydrogen bonds is changed, as by the substitution of deuterium for protium, then we can expect a percentage shift in the transition temperature of the order of the percentage shift in the strength of the hydrogen bonds. The formation and rupture of hydrogen bonds is just what is involved in the vaporization of water. For this process there is an overall difference in vapor pressure of 7 percent per hydrogen atom between protium and deuterium. This difference in vapor pressure would lead one to expect a shift of 21°C in transition temperature for a transition occurring near room temperature. A shift of 12°C in transition temperature has been found between deuterated and ordinary polybenzyl glutamate (*18*) (see Fig. 12). At any temperature the helical form is more stable for the deuterated compound than for the protium compound. This is a consequence of the greater stability of the deuterium bonds than of the protium bonds in hydrogen-bonded species. Similar results have been found with the enzyme ribonuclease. If enzymatic activity is dependent on the structure of the enzyme, deuteration can be expected to have profound effects on enzyme activity in some cases. The small shift in transition temperature can manifest itself in a qualitative difference in enzymatic behavior.

In addition to this effect of catalyst structure, we can expect rates and equilibria in deuterated media to be different from those in ordinary water. Mechanical properties such as viscosity are different in light and in heavy water. All these effects lead to differences in biological activity.

The general findings have been that growth rates are retarded in D_2O as compared with those in H_2O. It has been found possible to adapt lower animals from growth in H_2O media to growth in D_2O media, and vice versa. The change must be made slowly; even so, the morphology is considerably altered (*19*) (see Fig. 13).

In higher animals—for instance, rats—tolerance to 30 percent of D_2O has been established. Even with this concentration of D_2O the animals become quite sick after a month's exposure. The symptoms include considerable impairment of kidney function, anemia, disturbed metabolism, and altered adrenal function (*20*).

Summary

With the exception of the field of chemical kinetics, a brief survey has been presented of the principles of isotope chemistry and their utility in the ever-unfolding panorama of scientific research. We have come a long way since Soddy and Fajans arrived at the concept of chemical twins—isotopes. There are still places to go.

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Galileo's Discoveries in Dynamics

He left a mathematical stamp on nature still felt by physicists and natural philosophers.

Norwood Russell Hanson

Giants are frightening at close range. One views them with detachment only from far off. A giant within the history of science is no different. To give hindsight full play, we need to be 400 years distant from such an Olympian. How else can mere mortals take the measure of Galileo's mixture of imagination, intellect, and courage? (See *1*.) His contemporaries idolized him, or tugged back at his sandals, depending on whether they were frightened or inspired. At our remove fright is no longer likely. But even inspiration must be restrained for complete objectivity. Centuries of scholarship to the contrary notwithstanding, Galileo was not a great experimental scientist. He was no experimental scientist at all, not as we would know one. Nor was he a powerful theoretical thinker—surely not within technical mechanics. But he left a mathematical stamp on nature, the full imprint of which is still felt by physicists and natural philosophers.

Let me urge these theses seriatim: first, that Galileo was no experimentalist.

Experimental Scientist?

My first exposure to Galileo was to Galileo as "the father of experimental science." Apparently he was the first fully to appreciate precise laboratory measurement, careful experimental con-

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The author is professor of philosophy at Yale University, New Haven, Conn. This article is adapted from a lecture delivered 10 September 1964 at the University of Rochester, Rochester, N.Y., in honor of the 400th anniversary of the birth of Galileo Galilei.