DEUTERIUM AS A RESEARCH TOOL IN THE PHYSICAL AND BIOLOGICAL SCIENCES

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The discovery (1) of deuterium and the production of "heavy water," its chief compound, in a nearly pure state (2), are among the more important scientific achievements of recent years. In less than two years from the production of heavy water in nearly pure condition over three hundred papers reporting investigations *on* or *with* deuterium have appeared in scientific journals. While most of these investigations have been of a physical or chemical nature significant results have been reported in investigations of biological character. It is probable that the principal role of deuterium, in future research in all of these fields, will be more that of a research tool than as an object of investigation.

Deuterium is not a new chemical element, as the name might imply, but is a special variety of hydrogen atom. It differs from the ordinary (or light) hydrogen, chiefly, in mass. The atomic weight of the ordinary hydrogen is *one* while that of deuterium, or heavy hydrogen, is *two*. It resembles the ordinary hydrogen atom in possessing just one unit of positive charge on its nucleus (equal to the number of electrons in the neutral atom) and it is this latter property which determines the chemical character of an atom, and hence its position in the family of elements. The existence of atoms which differ in mass although alike in nuclear charge is common among the elements, and atomic species which are related in this manner are called isotopes. Isotopes are very difficult to separate, because they are so nearly identical in chemical behavior. Only with hydrogen in recent months have isotopic separations on a moderate scale been at all successful. The fact that this has been accomplished rather readily has made the special name, *deuterium*, advisable.

The chemistry of deuterium is, in the main, that of ordinary hydrogen. It is thus possible to have any of the hydrogen bearing compounds, so numerous in Chemistry, with one or more deuterium atoms replacing a corresponding number of ordinary hydrogen atoms. With water this leads to the two

possibilities HOD (D is the symbol which chemists employ to represent an atom of deuterium) and DOD. Pure "heavy water" consists of DOD alone, while heavy water of less than 100% purity consists of HOH, HOD, and DOD mixed in proportions which depend on the relative numbers of H and of D atoms in the mixture. In like manner three "heavy" ammonias—NH_2D, NHD_2 and ND_3—are possible and numerous deuterium derivatives of such molecules as benzene, C_6H_6; ethyl alcohol, C_2H_5OH; etc., can be produced.

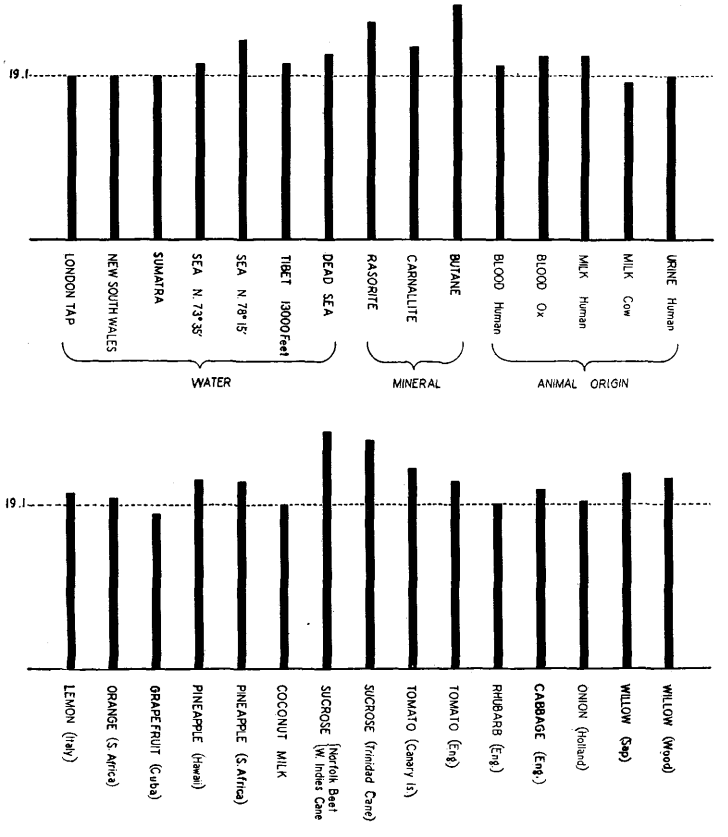


FIG. 1. (*Upper.*) Deuterium Content of Water from Natural Mineral and Animal Sources (relative to ordinary water).

FIG. 2. (*Lower.*) Deuterium Content of Water Obtained from Various Vegetable Sources (relative to ordinary water).

Replacement of light hydrogen in a molecule, by deuterium, necessarily results in an increase in the molecular weight—one unit for each replacement. Thus, for the respective molecules H_2O, HDO and D_2O molecular weights are 18, 19 and 20.

Molecular *volumes* are scarcely influenced by the replacements. As a result the *densities* of deuterium compounds are higher than for the corresponding compounds of ordinary hydrogen, and are in proportion to the molecular weights. The density of pure heavy water is very close to (20/18) times that of ordinary water and for less than 100% purity the density is a nearly linear function of the deuterium content. This provides one of the most convenient, as well as most accurate, ways of analyzing a sample of water for its deuterium content.

Deuterium exists in natural ground water to the extent of one D atom to about every 5800 H atoms (3) and contributes, through its presence, about 19.1×10^{-3} milligrams to the weight of each cubic centimeter of water. This proportion of D to H atoms is maintained, to a first approximation, in other natural sources but careful analyses reveal definite changes in the ratio which are characteristic of the nature of the source. The proportions of deuterium in waters derived from several mineral, vegetable and animal origins (4, 5, 6) is represented graphically in Figures 1 and 2 in which the dotted line (norm) corresponds to the deuterium content of normal ground water. Some of these variations in the ratio must be attributed to partial separations of the isotopes during chemical changes within living organisms—others to physical processes, such as evaporation.

The chemist does not *make* either deuterium or heavy water in the strict sense but is able to extract it from those natural sources—principally water—in which it already exists in low proportion. The high cost of heavy water is a consequence of the high cost of extraction and is not due to limitation of the gross supply. Indeed the potential supply of deuterium is inexhaustible. A simple calculation, based on the ratio of 1 D atom to every 5800 H atoms, reveals that enough deuterium is present in the circle of ocean visible from the deck of a large ocean liner to yield nearly one cubic mile of pure heavy water. By the cheapest process yet developed the cost of extracting this quantity of D_2O would require a ten billion dollar annual expenditure for a period of 800,000 years. There is little doubt that the cost of extraction will continue to drop, as it has done rapidly during the past two years. In this period the cost of pure D_2O has dropped from $150 per gram to about $2.00 per gram.

Heavy water is ordinarily produced by a process of electrolysis. Figures 3, 4, and 5 are views of portions of the

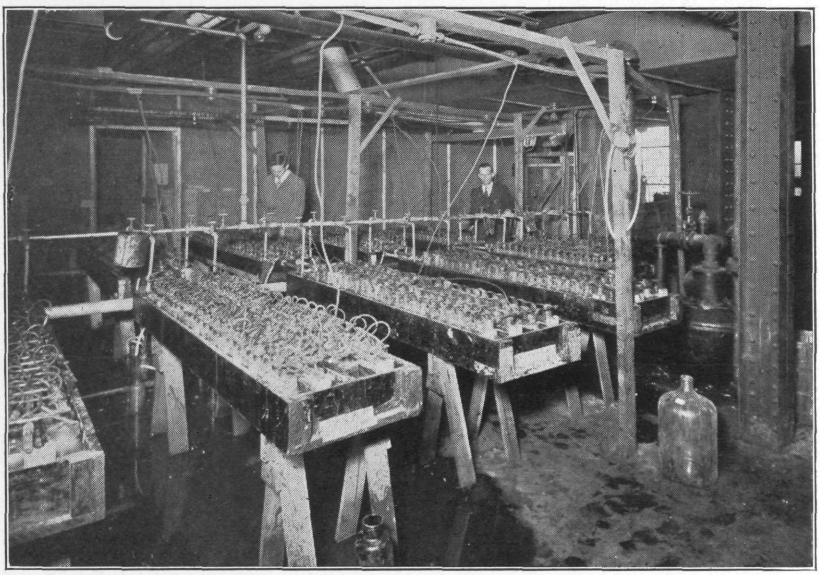


FIG. 3. Main Section of the Heavy Water Plant at the Ohio State University; 1000 water-cooled cells reduce 100 gallons of dilute heavy water from commercial cells, per week, to about 11 liters of 1% D_2O.

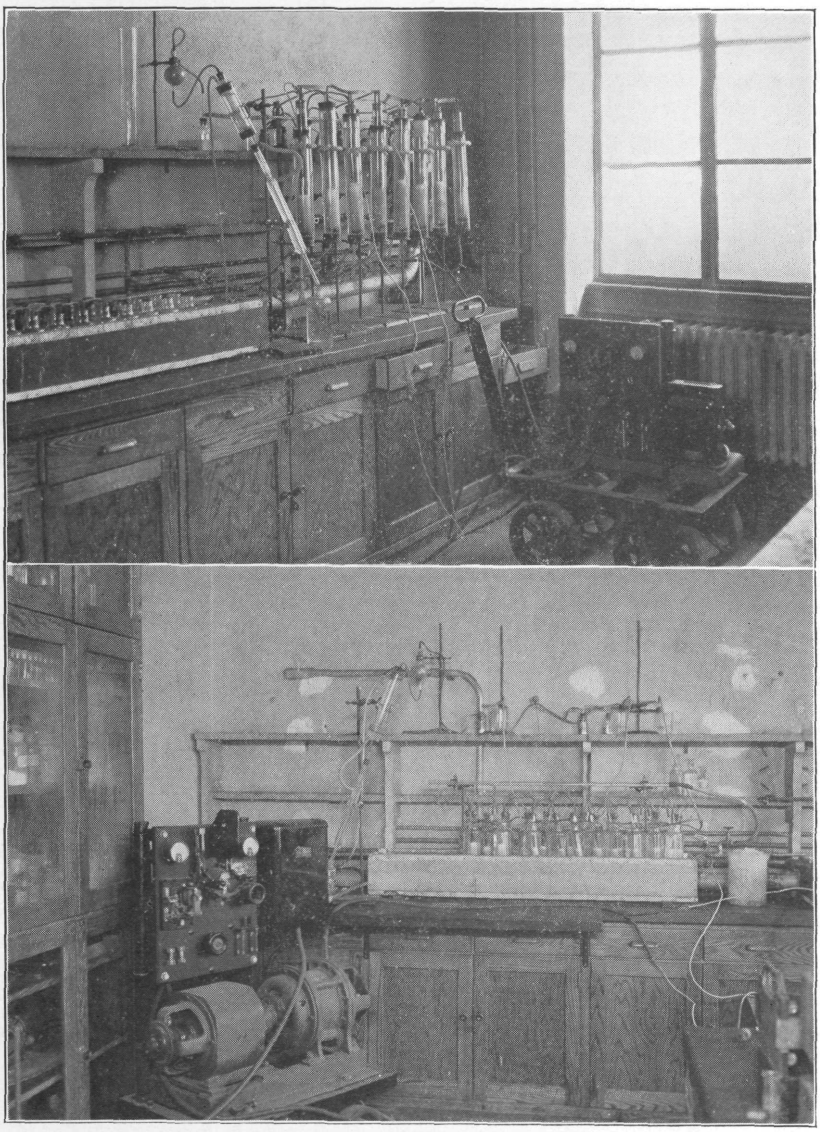


FIG. 4. (*Upper.*) Intermediate Section of the Heavy Water Plant at the Ohio State University. These cells of high current carrying capacity reduce the output of the Main Section to 10% D_2O. A burner and condenser for recombination of the electrolytic gases is shown in the foreground.

FIG. 5. (*Lower.*) Final Section of the Heavy Water Plant at the Ohio State University. These "test tube" cells reduce the output of the Intermediate Section to D_2O of concentration higher than 99%. The output is about 50 grams per week.

large heavy water plant constructed and operated at The Ohio State University,[1] which is capable of producing about fifty grams of pure D_2O per week at a cost of a little over $2.00 per gram. The use of the electrolytic process depends upon the fact that the H/D ratio in the hydrogen evolved in the electrolysis is 4 to 8 times larger than that in the electrolyte. As a consequence the concentration of deuterium in the residue increases as the electrolysis continues and approaches 100% as the volume of residue shrinks to zero. The efficiency of the process depends on the choice of electrodes and of electrolyte and on other conditions of operation.

Other methods may also be used to effect the extraction of deuterium. Distillation of water (7, 8) may in time replace the electrolytic process. Distillation of liquid hydrogen (1, 9) should be still more effective. Its principal hindrances are of an engineer-

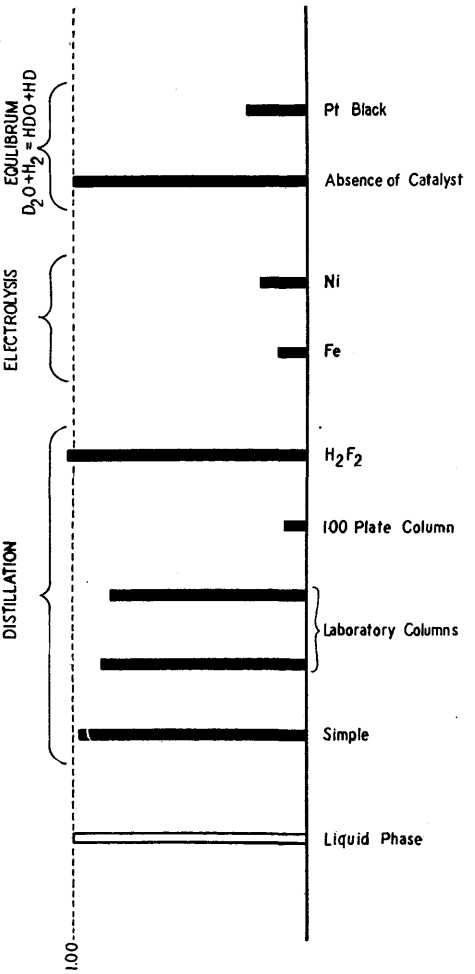


FIG. 6. Relative Efficiencies of Several Means of Separating Deuterium from the Lighter Isotope of Hydrogen. The heights of the vertical bars represent the deuterium content of the gas escaping from a liquid residue whose hydrogen is 1% deuterium.

[1]This plant was put into operation in March, 1934. The first and largest unit consists of approximately 1000 small water cooled cells constructed from ordinary 500 cc. wide-mouthed bottles closed with two-hole rubber stoppers and fitted with electrodes of Armco iron. The mixture of hydrogen and oxygen produced in the later stages of the electrolysis is allowed to recombine to reform water which is then electrolyzed over again, in an earlier stage of the plant, to recover the deuterium in the electrolytic gases. The raw material used in this plant was water taken from commercial electrolytic cells (D/H ratio, about 1/2000) and was furnished, free of charge, by the Capital City Products Co. of Columbus. The staff and students of the department of Chemical Engineering at

ing character and can, no doubt, be overcome. Diffusion (10) and desorption (11) processes and chemical reactions (12, 13) that liberate hydrogen or its gaseous compounds represent yet other ways of separating deuterium from its more plentiful isotope. Relative efficiencies of a number of these methods are

TABLE I

COMPARISON OF SOME PROPERTIES OF NORMAL WATER WITH THOSE OF PURE HEAVY WATER (COLLECTED FROM VARIOUS SOURCES)

	H_2O	D_2O
Molecular Weight	18	20
Specific Gravity	1.0000	1.1079
Freezing Point	0° C.	3.80
Boiling Point	100° C.	101.42
Refractive Index	1.33300	1.32828
Dielectric Constant	81.5	80.7
Viscosity (30°)	8.00	9.72
Heat of Fusion	1435	1510
Heat of Vaporization	10484	10743
Ionization Constant	1×10^{-14}	0.3×10^{-14}

Vapor Pressure Ratio (pH_2O/pD_2O) ≈ 1.05 at 100° C.
Solvent Action Toward Salts—Solubility in D_2O 80% to 90% of that in H_2O.

TABLE II

COMPARISON OF SOME PROPERTIES OF MOLECULAR HYDROGEN WITH THOSE OF PURE DEUTERIUM (COLLECTED FROM VARIOUS SOURCES)

	H_2	D_2
Molecular Weight	2.0156	4.027
Freezing Point	13.92° K.	18.58° K.
Boiling Point	20.38° K.	23.5° K.
Heat of Fusion	28.0 cal/mole	47.0 cal/mole
Heat of Vaporization	217.7 cal/mole	308.3 cal/mole
Heat of Dissociation (into atoms)	102,800 cal/mole	104,425 cal/mole
Viscosity (gas at 30° C.)	916 c. g. s. units	129.5

illustrated in Figure 6. Indeed, it is difficult to find a process —physical or chemical—in which measurable change in the proportion of the hydrogen isotopes is not produced.

The Ohio State University assisted in the preliminary preparations by distilling the water out of the strong alkaline electrolyte which was used in the commercial cells, and preparing fresh electrolyte for return to the Capital City Products Co. Dr. J. H. Koffolt was in immediate charge of this operation. The construction and operation of the heavy water plant was carried out with the assistance of Mr. W. H. Hall, graduate student in the Department of Chemistry.

Table I is a comparison of a few of the properties of pure D_2O with those of H_2O.

Table II is a similar comparison of molecular hydrogen with molecular deuterium, and Figure 7 illustrates the heat capacity vs. temperature curves (14) of the respective molecules H_2, HD and D_2. Other compounds of hydrogen would exhibit similar variation in properties from those of their deuterium analogues. In general the differences in properties are greatest at low temperatures.

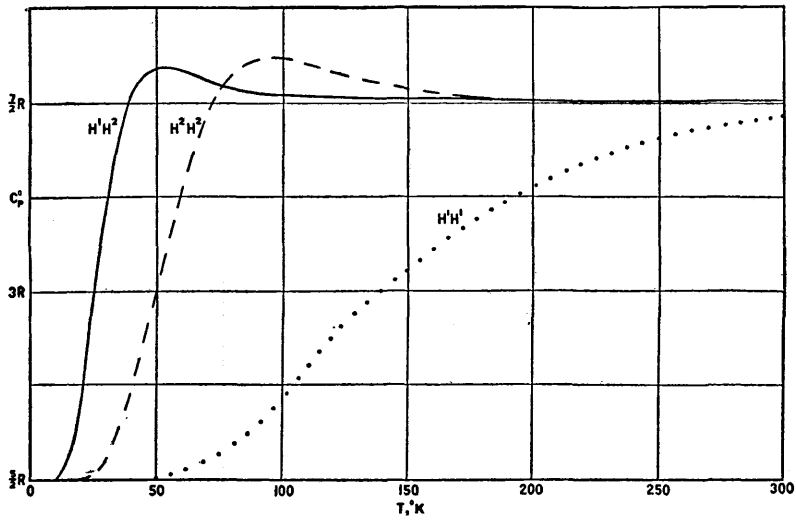


FIG. 7. Heat Capacity Curves (non equilibrium mixtures with respect to ortho-para states of D_2 and H_2) of H_2, HD and D_2. (After Johnston and Long, J. Chem. Physics **2**, 389 [1934].)

The utility of deuterium in research depends, in the majority of cases, directly or indirectly on variations such as are exhibited in Tables I and II or on quantitative estimates of the presence of deuterium, which utilize certain of these properties. Measurements of specific gravity (21, 15) or of refractive index (15, 16, 17) of carefully purified samples of water constitute the more usual and more accurate means of analyzing for deuterium but the measurement of the thermal conductivity (18) of gaseous mixtures of hydrogen and deuterium is not infrequently employed. The latter method is based on the differences in specific heat (Figure 7) on which thermal conductivity is dependent, and possesses the advantage that very tiny amounts of gas may be analyzed by this method.

It is possible, in this address, to illustrate the use of deuterium as a tool in solving fundamental problems in scattered fields for only a few of the cases in which it has been so employed. But these can be chosen to illustrate its wide range of applicability. For convenience I shall discuss these under the several headings of Physics, Chemistry, and the Biological Sciences.

PHYSICS

Modern Physics is concerned primarily with the structure of matter. This includes both the atom and the molecule and, more recently, attention has been turned to the tiny and almost inaccessible nucleus of the atom. Great progress has been made in nuclear investigations since the discovery of deuterium and the use of the deuteron, its own nucleus, to bombard the nuclei of heavier atoms or to produce *neutron* beams (19) of high intensity for the bombarding projectiles. This has resulted, in the brief space of two years, in the production of new radioactive substances (20) which possess utility as radioactive indicators in various types of chemical investigations and are sufficiently active to compete with natural radioactive elements in the treatment of disease. Continued progress in this field of nuclear investigation—with deuterium an indispensable tool—must inevitably result in a nuclear chemistry of far-reaching consequences and may unlock vast new storehouses of energy.

The greatest impetus to modern physical research came in Bohr's well known theory of the hydrogen atom. Although this theory broke down, in its details, when applied to the heavier elements it yielded, with Sommerfeld's modification, good quantitative agreement with all experimental observations of hydrogen itself. This theory of Bohr predicts very definitely the positions of lines in the spectrum of atomic deuterium. These lines should appear slightly shifted from the corresponding lines of ordinary hydrogen and the amount of the shift is calculable in terms of the theory. It is therefore of considerable interest that the discovery (1) of deuterium was based on the presence of weak lines at the positions calculated for an hydrogen atom of mass two (cf. Figure 8) and that further research (2) with much richer mixtures of deuterium and with higher dispersion in the optical systems (cf. Figure 9) were in good accord with the quantitative aspects of the simple Bohr theory. One

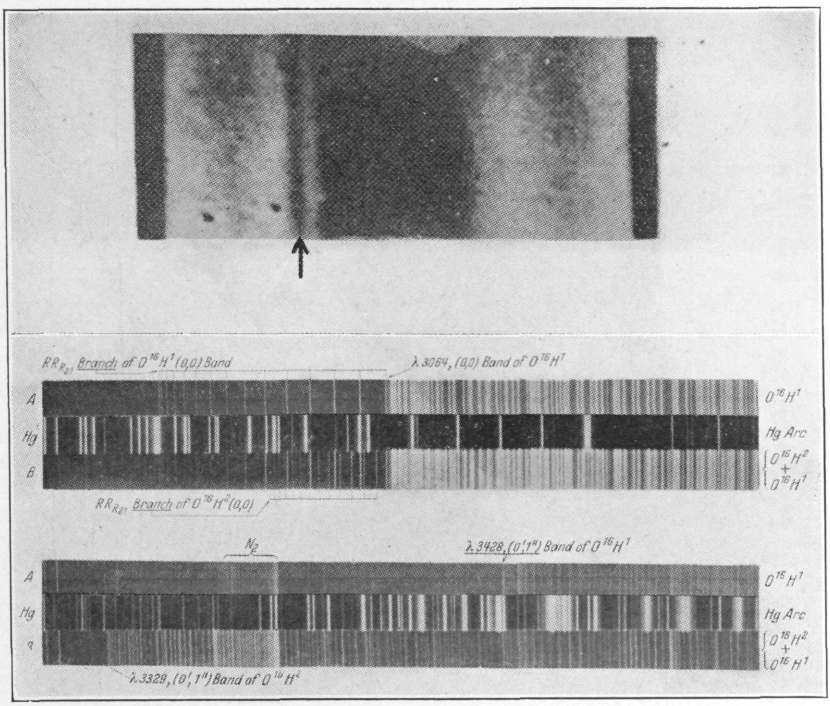


FIG. 8. (*Upper.*) Isotope Shift in one of the Balmer lines of Hydrogen (after Urey, Brickwedde and Murphy, Phys. Rev. **40,** 1 [1932]). The narrow line above the arrow is due to the D atom in hydrogen gas enriched slightly in deuterium by evaporation of liquid hydrogen.

FIG. 10. (*Lower.*) Isotope Effect in the Spectrum of OH (after Johnston and Dawson, Naturwissenschaften **21,** 495 [1933]). (The center strips in each panel are spectra of the mercury arc used for reference.)

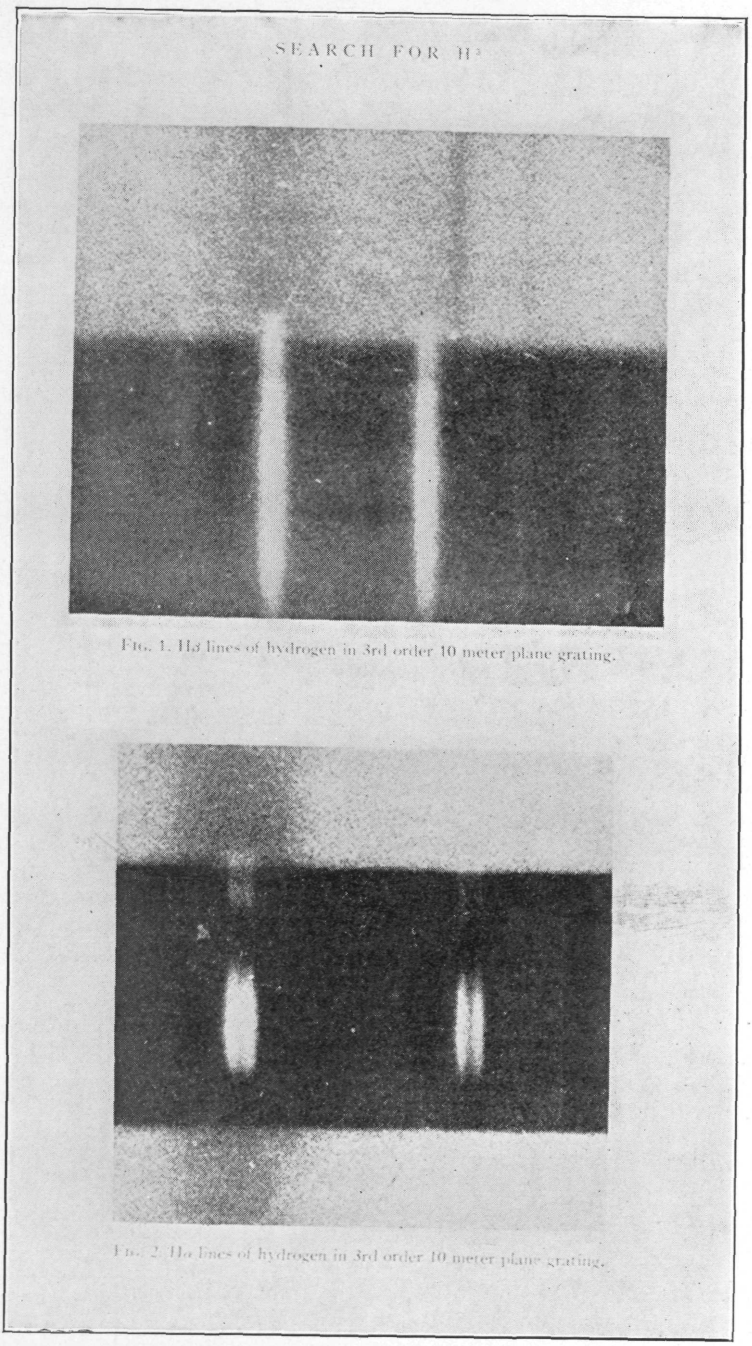


FIG. 1. Hβ lines of hydrogen in 3rd order 10 meter plane grating.

FIG. 2. Hα lines of hydrogen in 3rd order 10 meter plane grating.

FIG. 9. Wider Separation of the Isotope Lines due to atomic hydrogen with a nearly 50–50 mixture of H_2 and D_2. (After G. N. Lewis and F. H. Spedding, Phys. Rev. **43**, 964 [1933].) Note the sharper resolution of the doublet lines for one of the doublets on the lower photograph. This is the D line (these "lines" are really multiple) and is better resolved because of the smaller Doppler effect for the heavier atom.

quantitative feature of Sommerfeld's modified form of the Bohr theory, which involves the resolution of apparent single lines into several "fine structure" components, could never be tested adequately for ordinary hydrogen—due to overlapping and blurring of the component lines caused by the high velocity of hydrogen atoms moving in the region of the exciting discharge (Doppler effect). Simple gas kinetic theory indicates that the atomic velocities, and hence the blurring, should be less with deuterium than with hydrogen, so that this quantitative aspect of the Bohr-Sommerfeld-spin theory might now be subject to test. This is found to be true and investigations (22, 23) which may prove of considerable help in unravelling difficult aspects of atomic structure theory are in progress.

The structure of the molecule and the nature and magnitude of the binding forces which hold atoms together in individual molecules is a realm of great interest to chemists as well as to physicists. A great deal of progress has been made in this field during the past decade but there are still many problems unsolved even for the case of comparatively simple diatomic molecules. Knowledge in this field has come mainly through the study and interpretation of molecular spectra, commonly referred to as "band spectra," due to their characteristic appearance at low dispersion.

Errors in interpretation have arisen, not infrequently in the past, through failure to correctly identify the chemical nature of the molecule responsible for a spectrum. When it is possible to replace one atom in the responsible molecule by its isotope every line in its spectrum is shifted and the shifts on individual lines are calculable by theory. The use of this so-called isotope effect can therefore be employed sometimes to identify the chemical nature of the molecule responsible for a spectrum since the theoretical calculation of the shift depends on the correct chemical identification. An example of this kind (24) is illustrated in Figure 10. The spectra reproduced in this figure are emitted by water vapor through which an electrical discharge of high potential is passing and were variously assigned, in the early years of study, to the H_2O molecule and to the O_2 molecule. It was later interpreted as due to the unfamiliar gaseous molecule OH and these photographs obtained by passing an electrical discharge through a mixture of ordinary and heavy water definitely confirms this latter assignment. The RR lines whose positions are indicated on the bottom of

the (0, 0) band photograph and the λ 3329 band on the lower photograph fall very close to the positions calculated for an OD molecule. In this particular case the chemical identity of the molecule responsible for the water vapor spectrum was satisfactorily established beforehand but in the case of other molecules containing hydrogen—particularly molecules with more than two atoms—the isotope shift, with deuterium substitution, provides a means both of molecular identification and of the correct assignment of vibrational quantum numbers. Clues to the explanation of difficult points in the theoretical interpretation of complex molecular spectra and of the correct calculation of inner forces are also provided by exact quantitative measurement of the large isotope shifts in deuterium compounds and their departure from simple theory.

CHEMISTRY

Chemically, deuterium resembles ordinary hydrogen. However, this resemblance is not complete and small differences are found in equilibrium constants and, in several instances, rather large differences in reaction velocities. Perhaps the most important change in an equilibrium constant is that of the ionization constant of water to yield hydrogen and hydroxyl ions. For pure heavy water this important constant is about one-third (cf. Table I) of that for ordinary water, which indicates that the degree of ionization of D_2O is only 60% of that of H_2O. In a like manner weak acids or bases dissolved in D_2O ionize to a lesser degree (25) than in H_2O. The effect of these changes in important ionic equilibria is to change pH values and otherwise modify the character of certain ionic reactions in solution. Equilibrium changes of this character no doubt contribute to the biological effects of heavy water. A number of gas and gas-liquid phase equilibria whose constants show the isotopic influence on the reactivity have also been investigated, (26, 27, 28, 29, 14).

An interesting and important example of a chemical difference between deuterium and hydrogen compounds is furnished in displacement reactions of metals with water or with acid to yield gaseous hydrogen and in similar reactions which liberate gaseous compounds of hydrogen. The first examples of this sort were reported by A. and L. Farkas (12) and by Davis and Johnston (13) who observed, independently, that the gas liberated in reactions of this character, from solutions

which were a mixture of H_2O and D_2O, contained a lower proportion of deuterium than the solution from which it was liberated. The deuterium impoverishment in the gas stream is sometimes quite marked. The extent of this impoverishment is highly reproducible and is almost independent of the nature of the solution but is dependent on the surface character of the reacting metal. Figure 11 (30) illustrates the extent of this impoverishment for several reactions of this character. To what extent this effect may be attributed to changes in equilibrium constants and to what extent to differences in the reaction velocity of the heavy and light molecules or ions in the mixture is not yet known.

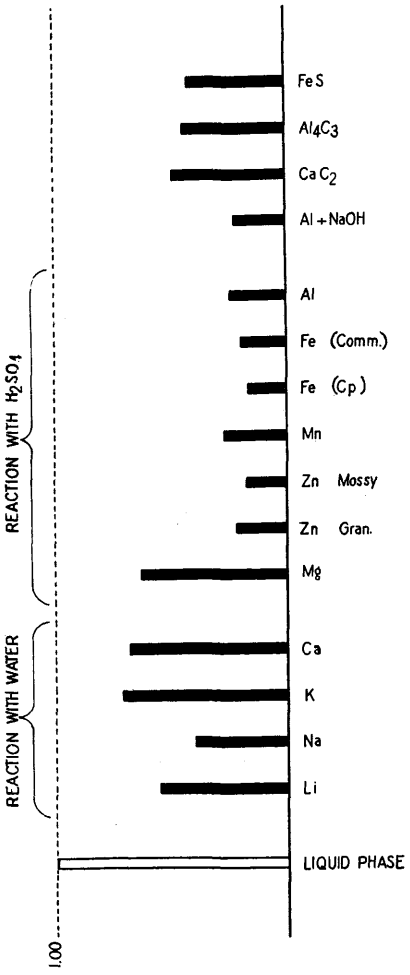


FIG. 11. Efficiency of several chemical replacement reactions in the separation of the hydrogen isotopes. The heights of the bars represent the deuterium contents of gas escaping from a liquid residue whose hydrogen is 1% deuterium. (Unpublished work of H. L. Johnston and C. O. Davis.)

A very simple type of reaction with isotopic atoms which is of great service in indicating the tightness of binding of various linkages and in studying chemical kinetics is of the type known as an "exchange" reaction. This type of reaction was first observed by Lewis (31) who observed that the hydrogen atoms in ammonia gas which was bubbled through a dilute heavy water solution "exchanged" with the hydrogen and deuterium atoms in the water (evidenced by the deuterium atom exchange) so that the deuterium concentration of the escaping ammonia approached that of the residual water. The mechanism of this exchange is represented by the following reaction:

$$NH_3 + HDO = NH_2D + H_2O \qquad (1)$$

which probably goes through the steps

$$NH_3 + HDO \rightleftharpoons NH_3DOH \rightleftharpoons NH_2D + H_2O \qquad (1a)$$
$$(\text{or } NH_3 + HDO)$$
$$\text{or } \rightleftharpoons NH_4OD \rightleftharpoons NH_3 + HDO.$$

With water containing a high concentration of deuterium, reaction of NH_2D may continue by a mechanism corresponding to (1a) until two or, finally, all three of the hydrogens of the original amomnia are exchanged with deuterium in the water. Likewise all four hydrogens in ammonium ion (NH_4^+) (32) and the acid hydrogen in strong acids (33) exhibit rapid exchange with water.

Interesting examples of exchange reactions between water and hydrogen of various linkages in organic compounds are shown in Table III, which is taken from the extensive review article of Urey and Teal (34).

TABLE III

EXCHANGE REACTIONS BETWEEN WATER AND ORGANIC COMPOUNDS

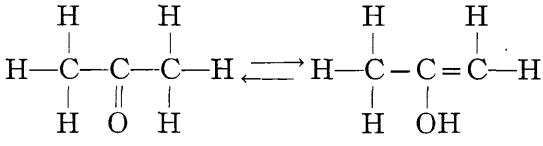
Compound	Observation	Reference
CH_3COONa	No exchange	(35)
CH_3COOH	1 hydrogen atom exchanges rapidly	(36)
C_6H_6	No exchange	(35)
CH_3CHO	1 hydrogen atom exchanges slowly	(35)
CH_2O	2 hydrogen atoms exchange slowly	(35)
CH_3COCH_3	Very slow exchange in neutral solution. Faster exchange in acid solution. Very fast exchange of all hydrogens in alkaline solution	(35, 37, 38)
$CH_3COCH_2COCH_3$	All hydrogens exchange	(35)
C_2H_2	Exchange in alkaline solution	(39)
Glucose and cane sugar	Hydroxyl hydrogen exchange immediately	(32)
$(CH_2OH)_2$	One-third of hydrogens exchange immediately	(33)
Egg Albumen	All hydrogens attached to N. atoms exchange	(40)
Cellulose	All hydroxyl hydrogens exchange	(40)

The several investigations included in this table show the immobility of hydrogen attached directly to carbon except where keto-enol transformations are possible; the high mobility of carboxyl, hydroxyl and amino hydrogen and the low mobility of aldehydo hydrogen. The exchange with acetylene in alkaline solution provides evidence for the weak acidic character of

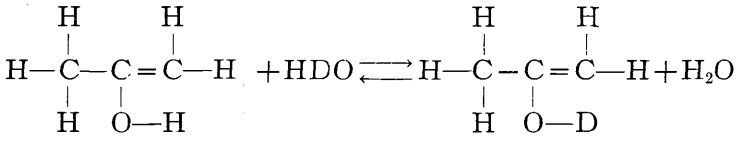
acetylene in aqueous solution, for which there was some evidence from other sources. This probably results from an equilibrium of the type.

$$C_2H_2 \rightleftharpoons C_2H^- + H^+ \qquad (2)$$

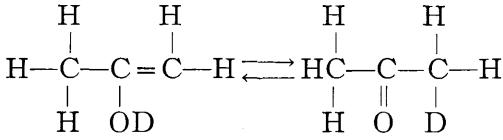
The exchange in acetone, in contrast to the resistance to exchange by methyl hydrogen in acetates and in acetic acid, is evidence in favor of the keto-enol transformation in acetone—a question which has been in dispute on the basis of direct chemical evidence alone. The exchange probably occurs with the hydroxyl hydrogen of the enolic form of the molecule and follows the following set of reactions.



(3a)



(3b)

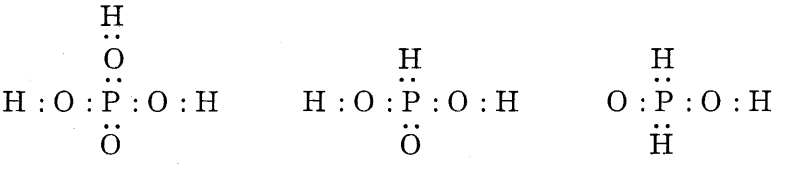


(3c)

This process may be repeated, in water of high deuterium content, until all six hydrogens of the acetone are replaced by deuterium.

A good example of the application of deuterium exchange reaction to problems of molecular structure is illustrated by the oxygen acids of phosphorus. Complete exchange of the three hydrogens in ortho phosphoric acid, H_3PO_4, takes place in line with the chemical expectation of complete hydrogen replacement to form the normal salts (e. g., Na_3PO_4) and illustrates that all three hydrogens in this molecule are attached by a mobile type of linkage. Two of the three hydrogens exchange in ortho-phosphorus acid (H_3PO_3) and only one of the three in hypo-phosphorus acid (H_3PO_2) (33). The immobility of a portion of the hydrogen in the latter acids points to a different type of linkage for the immobile atoms than that prevalent in

H_3PO_4. The structure of the latter molecule is characteristic of strong oxygen acids, such as sulphuric, and involves hydrogen linked to phosphorus, *through oxygen*. There are apparently only two such linkages in the H_3PO_3 molecule and only one such linkage in H_3PO_2. The probable structures of the three molecules based on the exchange phenomena is represented below.



H_3PO_4 H_3PO_3 H_3PO_2

The dots represent the position of bonding electrons which hold the atoms together. The immobile hydrogens are linked directly to phosphorus in a manner analogous to the immobile linkage direct to carbon in organic molecules. Latimer and Rodebush have previously postulated these structures for H_3PO_3 and H_3PO_2 on the basis of direct chemical evidence.

The most important results obtained through the use of deuterium in chemical research have been through its use as a tracer in chemical processes. The introduction of deuterium into a molecule provides a way of "labelling" the molecule which does not appreciably alter its normal chemical behavior. If deuterium be introduced at a definite position in an organic molecule the *normal* behavior of an hydrogen atom attached at that position, or of the group of which it is a constituent, during a chemical reaction, may be determined by tracing the deuterium through the products of the reaction. One excellent example of this use is in connection with determination of the mechanism by which ammonia decomposes in ultraviolet light. Stoichiometrically, the reaction is

$$2\,NH_3 + \text{ultraviolet light} = N_2 + 3H_2 \qquad (4)$$

and the first step is thought to be

$$NH_3 + \text{light} = NH_2 + H \qquad (4a)$$

The principal objection to this proposed mechanism is that only one-fourth as much NH_3 is decomposed for a given light absorption as is to be expected if this is the mechanism. This objection is over-ruled if it can be shown that the reverse

$$NH_2 + H = NH_3 \quad (4b)$$

reaction can occur spontaneously. Taylor and Jungers (41) have demonstrated, with the aid of deuterium that reaction (4b) does take place. They accomplished this by introducing deuterium atoms (produced by impacts of suitably energized mercury atoms on D_2 molecules) into dry ammonia gas and observing, by means of the spectrograph, the presence of NH_2D, of NHD_2 and of ND_3 molecules in the gaseous mixture. In the absence of direct exchange (no exchange occurs between dry NH_3 and D_2 in the absence of a catalyst) reaction (4b) is the only apparent mechanism which can account for the introduction of the deuterium. (The introduction of more than one atom of deuterium must have come about through repetition of reaction (4a) on ammonia molecules into which deuterium was already introduced by reaction (4b).

An unexpected reaction between ethylene and hydrogen, which is no doubt typical of other organic molecules with one or more double bonds, has been observed by Farkas, Farkas and Rideal (42) through a study of the reaction between ethylene and deuterium on the surface of a nickel wire. These authors find that both reactions

$$C_2H_4 + D_2 = C_2H_4D_2 \quad (5)$$

and

$$C_2H_4 + D_2 = C_2H_2D_2 + H_2 \quad (6)$$

occur simultaneously and by independent processes. Reaction (5) is the analogue of direct hydrogenation of the unsaturated molecule and is expected. Reaction (6), which predominates at temperatures above 60°C, represents a loosening of the C-H bond at the catalyst surface. This loosening, with exchange of atoms between the ethylene and hydrogen molecules undoubtedly occurs in mixtures of double bonded compounds with ordinary hydrogenation but is revealed, for the first time, through the deuterium tracer. An exchange of similar character between deuterium and the hydrogen in saturated aliphatic molecules does not occur at low temperatures but, through the tracer action of deuterium, Taylor and coworkers (43) have recently found evidence for exchange between methane CH_4, and deuterium at 170° C, on a nickel catalyst. The significance of this discovery is that it provides evidence for the breakdown of methane into the fragments CH_3 and H on a nickel catalyst at a temperature two hundred degrees lower than it has been possible to detect it by other means.

A particularly important result, from a practical standpoint has come about through a study of the exchange reaction

$$H_2 + D_2 = 2HD \qquad (7)$$

This reaction does not occur at all at moderate temperatures in the absence of catalysts. But in the presence of certain catalysts which are effective in commercial hydrogenation processes Gould, Bleakney and Taylor (44) find that the reaction takes place at temperatures even as low as that of liquid air. This reaction can only take place through the formation of atoms on the catalyst surface and the probable mechanism by which this occurs is illustrated in Figure 12.

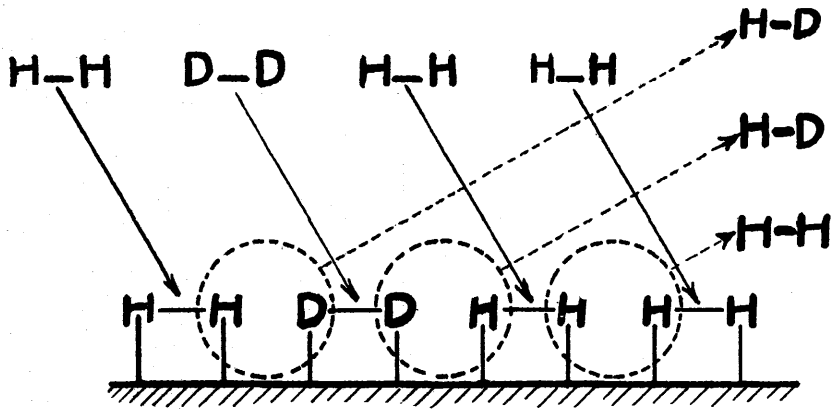


FIG. 12. Illustration of the probable manner in which the molecular bonds in H_2 and in D_2 are weakened on the surface of an hydrogenation catalyst so as to permit the re-pairing of atoms (or other rebonding of hydrogen atoms).

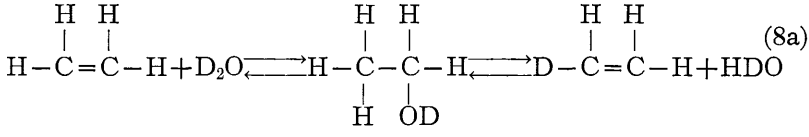
The figure is intended to show the way in which bonds established between the catalyst and the separate atoms weaken the bonds of atom to atom and permit return to the gas phase with an exchange of partners. This process—the loosening of hydrogen molecular bonds—is essential in many important industrial hydrogenation processes—such as the synthesis of ammonia from its elements. The experiments with deuterium show that the slow rate at which these commercial processes occur even at elevated temperatures is due to causes other than the loosening of the hydrogen bond, to which the slow reaction was previously attributed, and point the direction of future research.

The exchange reactions:

$$C_2H_4 + 2D_2O \rightleftharpoons C_2D_4 + 2H_2O \quad (8)$$

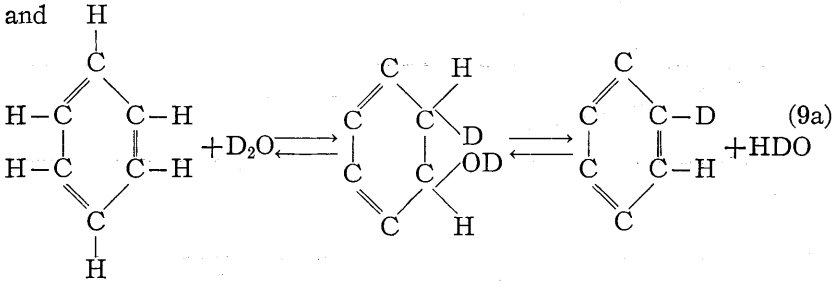
$$C_6H_6 + 3D_2O \rightleftharpoons C_6D_6 + 3H_2O \quad (9)$$

with liquid water occur only in the presence of sulfuric acid (45, 46). Polanyi (46) seeks to account for the influence of the acid by the mechanisms:



(8a)

and



(9a)

This proposal is the introduction of a water molecule into a double bond, in either case, and is the opposite of a dehydration process, for which sulfuric acid is very effective. Polanyi bases his proposal on the fact that a true catalyst promotes approach to an equilibrium condition from either direction. Further research will be necessary in this case to establish the true nature of the catalytic action of sulfuric acid but the possibility of some very interesting results in our understanding of the mechanism of catalysis is apparent.

Reaction velocities in processes which involve deuterium or its compounds generally differ from the velocities of the corresponding reactions with ordinary hydrogen. As a rule the effect of deuterium is to slow down the reaction. Figure 13 (47) illustrates this for the reaction of aluminum with sulfuric acid. In the case of certain of the simpler gaseous reactions it has been possible to correlate the velocity change, quantitatively, with the mechanism of the reaction. Thus for the reaction

$$H_2 + Br_2 = 2HBr \quad (10)$$

Bonhoeffer, Bach and Fajans (48) find that D_2 reacts five times more slowly than H_2 at 283° C. This is in good agreement with the 1600 calorie higher energy (Table II) required to dissociate D_2 for step (b) of the proposed mechanism

$$Br_2 = 2Br \qquad (10a)$$

$$Br + H_2 = HBr + H \qquad (10b)$$

$$H + Br_2 = HBr + Br \qquad (10c)$$

$$2Br = Br_2 \qquad (10d)$$

in which (10b) and (10c) constitute a "chain" broken by (10d), and (10b) is the rate controlling step in the mechanism. Melville (49) finds that the slower reaction rates of deuterium,

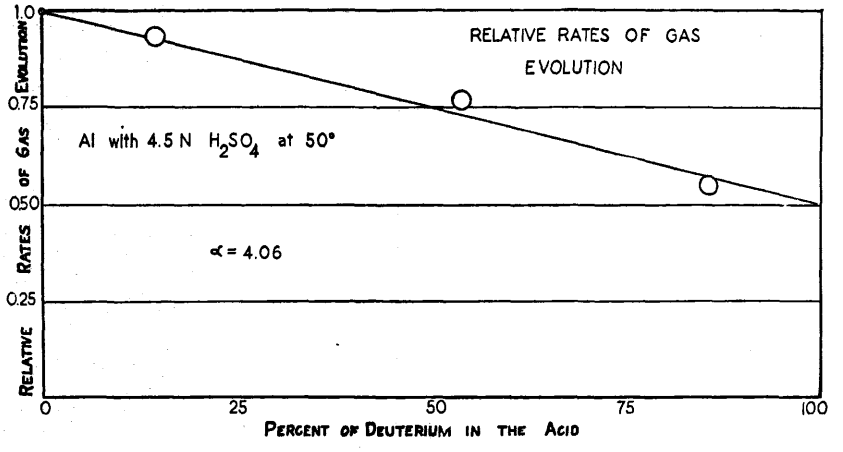


FIG. 13. Influence of Deuterium on the rate of reaction between Zinc and Sulfuric Acid. (Unpublished work of H. L. Johnston).

than of hydrogen, toward both O_2 and N_2O at the surface of a nickel catalyst are likewise in quantitative agreement with the difference in energies required to bind D and H atoms, respectively, to the catalyst surface.

A few examples have been found in which reaction rates with deuterium compounds proceed more rapidly than with ordinary hydrogen compounds (50, 51).

The use of deuterium as a tool in organic structural chemistry and mechanism—in which it should prove useful both as a tracer and as an indicator of the presence of groups which contain mobile hydrogen—is, as yet, scarcely touched.

BIOLOGY

Water with a high content of deuterium possesses a direct influence on certain physiological processes. Lewis (52) found that tobacco seeds fail to germinate in 80% heavy water (an excellent illustration of the results of this experiment, together with the 100% germination shown by controls, is given in the reference), and that the action of the heavy water is to inhibit or retard germination rather than to render the seed sterile (53). A similar inhibitory effect was observed for lupino seeds in dilute heavy water (54) but no effect whatever was observed on the germination of wheat (55). Taylor and his associates (56) have shown that high concentration of D_2O are fatal to tadpoles and to guppies within a few minutes and to lower organisms such as flatworms and protozoa within a few hours. Experiments of this sort have been frequently repeated by Taylor (57) with care exercised to eliminate every extraneous cause of the lethal action and the results reported in the original paper have been, each time, confirmed. Internal administration of nearly pure heavy water to a mouse (53), while not lethal in effect, did produce decided physiological reaction. This consisted of an increase in thirst and in a high excitability resembling intoxication.

The manner in which water with a high deuterium content is responsible for physiological changes is not known although there are several possibilities in view of the modifications of physical and chemical properties of water itself. These include: the change in the ionization constant of water and in the ionization and hydrolysis constants of dissolved electrolytes; unequal changes in the rate constants of various interdependent biochemical reactions taking place in the organism; the hydroscopic action of heavy water (i. e., its ability to absorb ordinary water from or through the tissues much as absolute alcohol would do) and changes in osmotic pressure. These possible causes of physiological modification are in addition to direct toxic effect of deuterium compounds themselves. It is unknown whether or not a direct toxic effect exists.

In addition to these investigations with whole organisms some significant results have been obtained in experiments on the metabolism of special cells in the presence of water having a high deuterium content. Drs. Doan, Wiseman and associates in Ohio State's Department of Medical Research (58) have made a quantitative study of the influence of both 7% and 50%

heavy water on the metabolism of white blood corpuscles, by means of a Warburg apparatus. They find marked decreases in the rate of respiration in the presence of heavy water, with the effect much greater for the 50% heavy water, although no effect was produced either on the rate of CO_2 metabolism or on

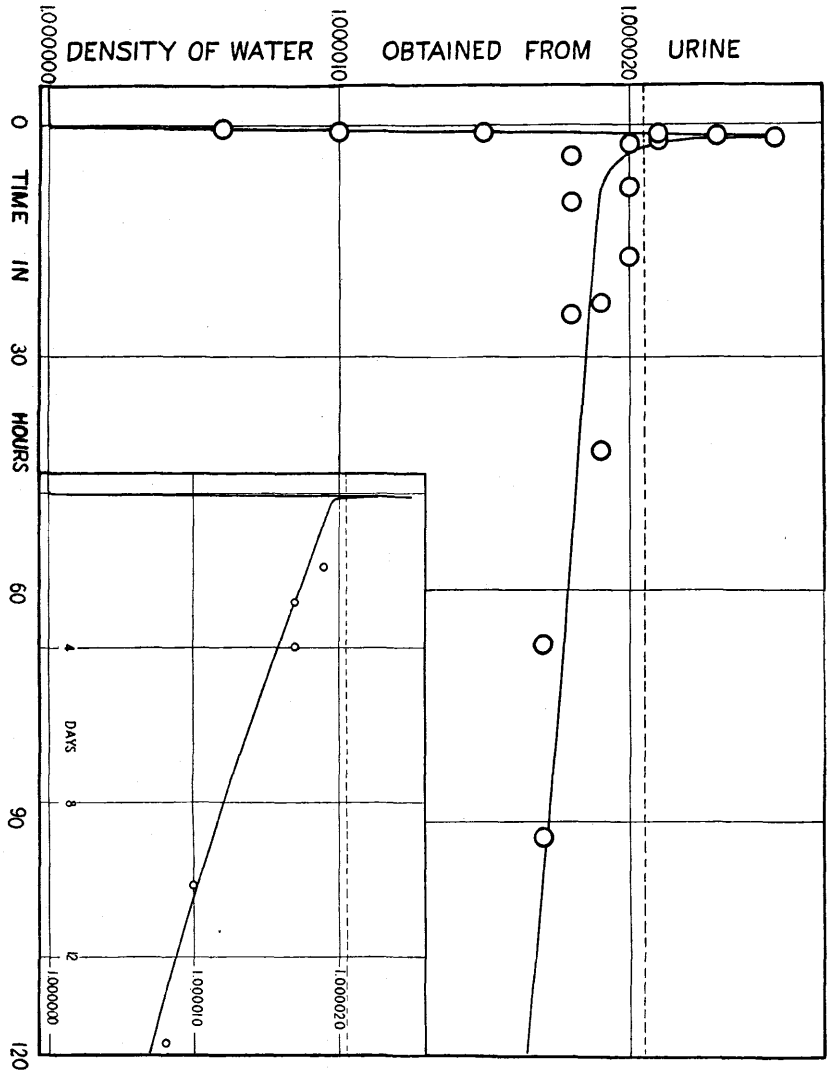


FIG. 14. Loss of Deuterium with urine following drinking of dilute heavy water. (Constructed from the data of Hevesy and Hofer.) The dotted line represents the specific gravity to be expected for water from a fluid produced by mixing two liters of 0.5% D_2O with 45 liters of ordinary water.

glycollosis. This result is interesting because natural causes which modify the respiration rate also modify CO_2 metabolism and glycollosis and the magnitudes of the several effects are usually related. Investigators at Princeton have also made extensive studies of the influence of D_2O on cell respiration and obtained smooth curves which relate the rate of respiration to the deuterium content of the water (59).

Pacsu (60) finds that the alcoholic fermentation of d-glucose in 95% heavy water proceeds nine times more slowly than in ordinary water, and in 60% heavy water with about two-thirds of the velocity in ordinary water. The fact that yeast which has first been cultured in 95% D_2O fails to regain activity when the culture solution is diluted to 45% D_2O shows that deuterium here exerts a permanent toxicity toward the zymase enzyme.

The tracer action of deuterium may be utilized in biological, as in chemical, research and it is probably safe to predict that this use in biological investigations opens a wider field for its utilization than the study of its direct physiological effects. An excellent example of this utilization is contained in the recent very interesting work of Hevesy and Hofer (61) who used deuterium to find how rapidly water taken internally becomes distributed through the human body. The experiment consisted in carrying out systematic deuterium analyses of the urine excreted by a person who drank two liters of water about 0.5% of whose hydrogen was deuterium. Figure 14 shows the results of the experiment. The ordinates measure the specific gravity of the water distilled from the urine. The abscissa represents the duration of the investigation. The two liters of 0.5% D_2O was taken at time zero. Analysis of the urine preliminary to the start of the investigation yielded normal water (cf. Fig. 2). The dotted line in the figure represents the specific gravity to be expected if the two liters of 0.5% heavy water were thoroughly mixed with the approximate 45 liters (two-thirds of body weight) of water present in the body. The figure shows that this distribution was attained in about three hours. One-half of the deuterium taken in the experiment was excreted in 10 days. Since this was excreted at the same rate as ordinary water in the body the conclusion can be drawn that one-half of the water contained in the human body (i. e., one-third of its weight) is replaced every 10 or 12 days. MacDougall and coworkers (62) found, in a similar experiment with rats, that one hour was sufficient to allow thorough mixing of the body water of the rat with water taken into the stomach.

By using foods or drugs in which ordinary hydrogen is replaced by deuterium so as to introduce the tracer it is obvious that deuterium may sometimes be used to obtain information on the nature and the rapidity of normal physiological processes.

CONCLUSION

References to many excellent pieces of research on or with deuterium have been necessarily omitted. The examples cited are sufficient to show the possibilities opened up by the use of deuterium as a tool of research and the wide range of research fields to which it is applicable. Research with deuterium requires, in the majority of cases, careful physical measurements of some type and ingenious utilization of the small differences which exist between isotopic species. Wider use of deuterium as a tracer, in various fields of research, appears to offer the greatest promise for more extended contributions to future research.

Deuterium is probably only a fore-runner of the use of other isotopes as research tools. The separation of oxygen isotopes has been partially accomplished and Polanyi and Szabo (63) have used the heavier isotope of oxygen as a tracer to determine the mechanism of ester hydrolysis. The complete or partial separation of other isotopes will probably soon be an accomplished fact. Developments of this character will not affect the simpler aspects of our chemistry. They will, however, equip us with yet more tools to attack the myriad problems of science.

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