

The same force constants were used as in BH_3 except for the force constant related to the out-of-plane vibration. The results of these calculations are summarized in Table I. The force

TABLE I

FUNDAMENTAL VIBRATIONAL FREQUENCIES OF BH_3 , BD_3 , BD_2D AND BH_2T ASSUMING VALENCE FORCES

Vibration	BH_3	Frequency (cm. ⁻¹) BD_3	BH_2D	BH_2T
ω_1	2310	1635	1756	1143
ω_2	1527	1190	2386	2377
ω_3	2470	1860	1156	767
ω_4	1190	872	1134	801
ω_5			2403	2391
ω_6			1418	1382

constants for the BH_3 and BD_3 cases are $k_1 = 3.16 \times 10^5$, $k_8/l^2 = 0.25 \times 10^5$ and $k_{\Delta}/l^2 = 1.08 \times 10^5$ dyne cm.⁻¹ for the stretching, bending in-plane and bending out-of-plane force constants, respectively. The same constants were used for the BH_2D and BH_2T with the exception of k_{Δ}/l^2 which was 0.86×10^5 dyne cm.⁻¹.

The vibrational and rotational constants of H_2 , HD , D_2 and HT were obtained from published literature.

Substituting this information into the basic equations, one obtains for experiments I and II

$$\left(\frac{R_{\text{T}}}{R_{\text{D}}}\right)^{\text{I}} = 2.0 \frac{k_8}{k_3} \text{ and } \left(\frac{R_{\text{T}}}{R_{\text{D}}}\right)^{\text{II}} = 4.3 \frac{k_8}{k_3}$$

In order to evaluate the ratio of the tritium to deuterium rates, one must evaluate the ratio of rate constants k_8/k_3 . This can be done in principle but in practice rather drastic assumptions have to be made. We have chosen therefore to obtain an approximate value of this ratio from experimental data. In the rate-determining step of the hydrogen-diborane exchange, borane forms a complex with diborane which is probably B_3H_9 and a terminal bond from the BH_3 becomes a bridge bond in the complex. In the $\text{B}_2\text{H}_8\text{-B}_3\text{H}_9$ exchange, again BH_3 interacts with B_3H_9 forming a complex which involves converting terminal bonds to bridge bonds. It is assumed that the magnitude of the

isotope effect in these two reactions is not very different. A normal isotope effect would be expected for both of these elementary reactions. In the $\text{B}_2\text{H}_8\text{-B}_3\text{H}_9$ exchange two steps are involved. One is the equilibrium process between BH_3 and B_2H_6 which in turn is followed by the rate-determining process in which the exchange takes place. An isotope effect is expected for the equilibrium process since the vibrational frequencies for the planar BH_3 are expected to be lower than those for diborane. Assuming that the magnitude of the isotope effect is about the same in each and since the over-all ratio of deuterium to tritium exchange is about 2.0 (see Fig. 2) in this reaction, a reasonable value for the ratio of the constants for the rate-determining steps k_3/k_5 is approximately 1.6. Applying these values to the cases in question, one obtains 1.3 and 2.7 for the ratio of tritium to deuterium rates for series I and II, respectively. These are to be compared with the experimental values 1.6 and 2.9, respectively. The agreement is as reasonable as one can expect and indicates that the magnitude of the inverse isotope effect observed for the hydrogen-diborane reaction is not incompatible with the proposed mechanism. It remains to make some comment on the origin of the observed weak surface dependence of this reaction. Marcus² obtained the following relation between the rate R and the elementary rate constants for the reaction sequence

$$R = \frac{k_2ca}{\frac{k_{-2}a/2}{k_6c + k_3b/6} + 1}$$

listed above. If one assumes that the chain-terminating step takes place at least partly on the walls, the magnitude of the surface effect expected from the above relation is not incompatible with the observed results.

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[CONTRIBUTION FROM ARGONNE NATIONAL LABORATORY, ARGONNE, ILLINOIS]

Primary and Secondary Deuterium Isotope Effects on Rate of Mutarotation of Fully Deuteriated Glucose and Mannose¹

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The rates of mutarotation of glucose, fully deuteriated d-glucose, d-glucose-1-d, d-mannose and fully deuteriated d-mannose in H_2O , D_2O and $\text{H}_2\text{O-D}_2\text{O}$ mixtures, and in the presence of 0 to 0.05 *M* perchloric acid, at 25°, have been studied. The decrease in rate in D_2O represents a primary isotope effect in that O-H and O-D bonds are broken and reformed. The secondary isotope effect on mutarotation is a consequence of the presence of C-D rather than C-H bonds in the molecule and also results in a decrease in the rate of mutarotation. For fully deuteriated glucose, the secondary isotope effect amounts to about 17% in water and about 16% in D_2O in neutral solution. The secondary isotope effect is essentially the same as for d-glucose-1-d, and may be accounted for by the supposition that the principal effect on the rate of mutarotation is due to the replacement of D for H in the carbon-hydrogen bond at carbon atom 1.

Introduction

Most hydrogen ion-catalyzed reactions are faster in D_2O than in H_2O .³ Moelwyn-Hughes and Bon-

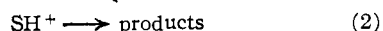
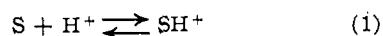
hoeffer⁴ have postulated the mechanism of specific acid catalysis to be

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(3) K. Wiberg, *Chem. Revs.*, **55**, 713 (1955).

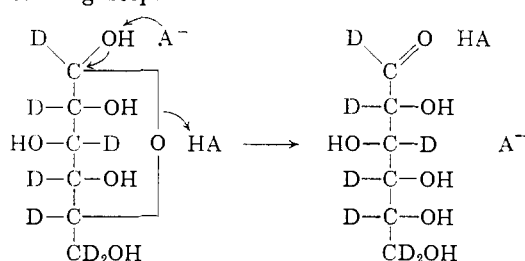
(1) Based on work performed under the auspices of the U. S. Atomic Energy Commission. Presented at the New York A. C. S. Meeting, Sept., 1960.

(4) E. A. Moelwyn-Hughes and K. F. Bonhoeffer, *Z. Elektrochem.*, **40**, 469 (1934); K. F. Bonhoeffer and O. Reitz, *Z. physik. Chem.*, **A179**, 135 (1937).



where S is the substrate. Since deuterium oxide is believed to be less basic than water,⁸ it appears reasonable that the substrate can compete with the solvent for the deuteron in D₂O more effectively than for the proton in H₂O. The concentration of the conjugate acid of the substrate, SH⁺, will then be higher in D₂O than in H₂O and consequently the rate of the reaction should be higher in D₂O than in H₂O, if the second step does not show an isotope effect.

The mutarotation of glucose is an early example of an acid-catalyzed reaction which proceeds more slowly in D₂O than in H₂O. Unlike the above reaction, this is a case of general acid-base catalysis, and its mechanism is believed to be that shown below, in which a proton is transferred from the acid to the substrate (α -D-glucose or β -D-glucose) and from the substrate to a base in the rate-controlling step.



(The mechanism is illustrated for the mutarotation of fully deuterated glucose in H₂O to emphasize the unique nature of the hexose.) Such a scheme is similar to the "concerted" mechanism proposed by Swain and Brown.⁵ The change from the α - or β -form of glucose to the aldehyde form is considered to be slow relative to the change from the aldehyde form to the α - or β -form. A normal isotope effect is found, since bonds to hydrogen or deuterium are broken and reformed in the rate-determining step and the values of k_{H_2O}/k_{D_2O} decrease with increasing strength of the acid when water, acetic acid and hydronium ion are compared.³ Challis, Long and Pocker⁶ interpret the solvent isotope effect on mutarotation somewhat differently, but the details of the mechanism are not the chief interest here.

In the present research, the rates of mutarotation of glucose, fully deuterated glucose (97–99% deuteration of all the non-exchangeable hydrogens and designated deuterio-D-glucose), mono-deuterated D-glucose-1-d, D-mannose and fully deuterated mannose (designated deuterio-D-mannose) were compared in different H₂O and D₂O media for the purpose of investigating the primary and secondary deuterium isotope effects. It had been reported⁷ previously that in deuterium oxide, glucose readily exchanges five of its hydrogen atoms. Since there are five OH groups in glucose

(5) C. G. Swain and J. F. Brown, Jr., *J. Am. Chem. Soc.*, **74**, 2534, 2538 (1952).

(6) B. C. Challis, F. A. Long and Y. Pocker, *J. Chem. Soc.*, 4679 (1957).

(7) E. A. Moelwyn-Hughes, R. Klar and K. F. Bonhoeffer, *Z. physik. Chem.*, **A169**, 114 (1934); W. H. Hamill and W. Freudenberg, *J. Am. Chem. Soc.*, **57**, 1427 (1935).

and mannose, this indicates that all hydroxyl hydrogens are readily replaceable with deuterium, and the non-exchangeable hydrogens are the seven atoms which are bonded directly to the carbon atoms. As has been pointed out by Hamill and LaMer,⁸ the rate of isotopic exchange must be appreciably greater than the rate of mutarotation of glucose, because otherwise the proportion HG/DG would change continuously during the mutarotation experiment in deuterium oxide and the rate constants of mutarotation would drift with time. In all of our experiments, no apparent drift of the rate constant k has occurred (k is constant to the extent of $\pm 0.5\%$ in a single experiment), and we conclude therefore that the exchange of hydroxyl hydrogens occurs much more readily than mutarotation of glucose and mannose. The formula of the fully deuterated glucose and deuterated mannose in aqueous media may therefore be written C₆D₇O(OH)₅; whereas in D₂O media the formula of glucose (mannose) and deuterated glucose (mannose) may be written C₆H₇O(OD)₅ and C₆D₇O(OD)₅, respectively. Similarly, D-glucose-1-d may be written C₆H₆DO(OH)₅ and C₆H₆DO(OD)₅ in H₂O and D₂O solutions.

Experimental

Materials.—Deuterio-D-glucose and deuterio-D-mannose were isolated from fully deuterated green algae grown in 99.6% D₂O as described by Crespi, Conrad, Uphaus and Katz.⁹ The hexoses are isolated by column chromatography on cellulose from the acid hydrolysate of the cell walls of fully deuterated algae; details of the isolation procedure are given elsewhere.¹⁰ Analysis of the water of combustion of the deuterio-D-glucose indicated that the deuterium content of the non-exchangeable hydrogen positions was 97–99% deuterium.

D-Glucose-1-d was supplied through the courtesy of Dr. Louis Kaplan of this Laboratory. The compound had been prepared by conventional procedures by reduction of D-glucono-lactone in D₂O with sodium amalgam. The isotopic purity of the 1-d position was greater than 98% deuterium. The ordinary glucose used in the present experiments was Mallinckrodt analytical reagent grade. All of the hexoses were purified by recrystallization and were chromatographically pure.

Heavy water was of better than 99.6% D₂O content. It was purified by distillation from alkaline permanganate in a Barnstead conductivity-water still. Dilute solutions of DClO₄ were prepared by pipetting the proper amount of 70% HClO₄ into D₂O and the composition of the acid checked by the usual procedures. For the low concentrations used in the present work the added hydrogen did not alter the deuterium content by a significant amount.

Measurements.—Rotations were measured with a Rudolph Model 200 photoelectric polarimeter operating from a xenon arc lamp. Water was circulated through

TABLE I

ACID CATALYSIS OF THE MUTAROTATION OF DEUTERIO-D-GLUCOSE IN AQUEOUS AND DEUTERIUM OXIDE MEDIA, 25°

HClO ₄ , M	k , min. ⁻¹	DClO ₄ , M	k , min. ⁻¹
0.0001	0.0088	0.0000	0.0025
.0100	.0118	.0080	.0040
.0140	.0125	.0190	.0062
.0250	.0155	.0331	.0080
.0300	.0161	.0470	.0113
.0470	.0214	.0504	.0121

(8) W. H. Hamill and V. K. LaMer, *J. Chem. Phys.*, **4**, 395 (1936).

(9) H. L. Crespi, S. M. Conrad, R. A. Uphaus and J. J. Katz, *Ann. New York Acad. Sci.*, **84**, 648 (1960).

(10) M. I. Blake, H. L. Crespi, V. Mohan and J. J. Katz, *J. Am. Pharm. Assoc., Sci. Ed.*, in press.

TABLE II
 VALUES OF THE CONSTANTS OF EQUATION 4, 25°^a

Substrate	In H ₂ O		In D ₂ O	
	<i>k</i> ₀	<i>k</i> ₁	<i>k</i> ₀	<i>k</i> ₁
D-Glucose	0.0102	0.283 ± 0.003	0.0029	0.208 ± 0.005
Deuterio-D-glucose	.0087	.270 ± .007	.0025	.190 ± .004
D-Glucose-1- <i>d</i>	.0091	.260 ± .004	.0025	.198 ± .006
D-Mannose	.0292	3.56 ± .05	.0093	3.36 ± .08
Deuterio-D-mannose	.0266	3.11 ± .09	.0087	2.67 ± .06

^a *k* is defined by equation 3. Units are min.⁻¹ for *k* and *k*₀, and liters/mole min. for *k*₁.

10 and 20 cm. tubes, with glass end plates, from a bath maintained at 25.0°. The runs showed excellent first-order dependence over two half-lives, and the rate constants were independent of whether 5893 or 3600 Å. wave length light was used. We have found that the angle of rotation at 3600 Å. is about 2.75 times larger than the rotation at 5893 Å. and, because of the limited amount of deuteriated glucose available, most of the runs were made at 3600 Å.

Results and Discussion

The rate constant of mutarotation *k* is given by the equation

$$k = \frac{1}{t} \log \frac{R_0 - R_\infty}{R_t - R_\infty} \quad (3)$$

where *t* is time in minutes and *R* is angle of rotation. Plots of log (*R*_{*t*} - *R*_∞) vs. *t* give straight lines, and the rate constant *k* is reproducible to ± 2%.

The rates of mutarotation of glucose, deuterio-D-glucose, D-glucose-1-*d*, mannose and deuterio-D-mannose, in the presence of 0 to 0.05 *M* perchloric acid at 25°, have been measured in aqueous and deuterium oxide media. As examples, the rate constant data for the mutarotation of deuterio-D-glucose in aqueous and deuterium oxide media are given in Table I and the values of various constants are assembled in Table II. Linear plots of the observed rate constants for glucose and mannose vs. the molarity of the acid catalyst, HClO₄ or DCIO₄, are obtained. The straight lines follow the equation

$$k = k_0 + k_1(\text{H}_3\text{O}^+) \quad (4)$$

For glucose in aqueous media and 25°, Kuhn and Jacob's equation¹¹ is $k = 0.0104 + 0.334(\text{H}^+)$, and Hudson's equation¹² is $k = 0.0096 + 0.258(\text{H}^+)$. For mannose in aqueous medium at 24.8°, Hudson and Sawyer¹³ found $k = 0.0291$. For glucose-1-*d* at 24°, Bentley and Bhate¹⁴ found *k*₀ to be 0.00913 and 0.00241 in H₂O and D₂O, respectively. In order to demonstrate the primary and secondary deuterium isotope effects on the mutarotation, we have assembled certain ratios of the constants in Tables III and IV.

The values of *k*_H/*k*_D in Table III represent primary deuterium isotope effect on the rate of mutarotation in that the O-H and O-D bonds are broken and reformed in the rate-determining step. It is interesting to note in this connection that Nicolle and Weisbuch¹⁵ have listed the values of *k*_{H₂O} and *k*_{D₂O} at 18–20° to be between 3.0 and 3.8 for glucose, galactose, xylose, arabinose, sorbose, lactose and maltose. The value of *k*_{H₂O}

TABLE III

PRIMARY DEUTERIUM (SOLVENT) ISOTOPE EFFECT ON MUTAROTATION OF GLUCOSE AND MANNOSE, 25°

	Catalyst	This work	<i>k</i> _{H₂O} / <i>k</i> _{D₂O}	
			Lit. values	
D-Glucose	H ₂ O	3.52	3.80 (3.16) ³ ; 3.56 ¹¹ (23°); 3.2 ^a	
	H ₃ O ⁺	1.36	1.37 ³ ; 1.31 ^a	
Deuterio-D-glucose	H ₂ O	3.48		
	H ₃ O ⁺	1.42		
D-Glucose-1- <i>d</i>	H ₂ O	3.64	3.78 ¹¹ (24°)	
	H ₃ O ⁺	1.31		
D-Mannose	H ₂ O	3.14		
	H ₃ O ⁺	1.06		
Deuterio-D-mannose	H ₂ O	3.06		
	H ₃ O ⁺	1.16		

^a Values for tetra-O-methylglucose, ref. 6.

*k*_{D₂O} for tetra-O-methylglucose is included in Table III. According to Challis, Long and Pocker,⁶ the principal isotope effect on the rate of mutarotation is due to the replacement of D for H on the -OH group at the reaction center (at carbon atom 1), the isotope effect of the four exchangeable hydrogens remote from the reaction center being small. This would account for the similar primary isotope effect found for glucose and for tetra-O-methylglucose.

The values of *k*_H/*k*_D in Table IV are calculated from the values of *k*₀ and *k*₁ listed in Table II and represent a secondary deuterium isotope effect, because the difference between glucose and deuteriated glucose in a given medium lies simply in the difference between C-H and C-D bonds. Since these bonds are not broken in the reaction, the small magnitude of the secondary isotope effect is reasonable. Thus, a secondary isotope effect very similar in magnitude is observed in the solvolysis of methyl tolyl carbonyl chlorides,¹⁶ and a number of workers¹⁷ have observed that α-deuterium substitution causes a slowing of a carbonium ion solvolysis reaction by about 15%. The secondary isotope effect observed in the mutarotation of deuteriated hexoses is thus quite comparable to many secondary isotope effects that have been observed in other reactions.

Table IV indicates that the secondary isotope effect for deuterio-D-glucose and for D-glucose-1-*d* is the same. Essentially the entire secondary isotope effect on the rate of mutarotation arises from the replacement of hydrogen by deuterium

(11) R. Kuhn and P. Jacob, *Z. physik. Chem.*, **113**, 389 (1924).

(12) C. S. Hudson, *J. Am. Chem. Soc.*, **29**, 1571 (1907).

(13) C. S. Hudson and H. L. Sawyer, *ibid.*, **39**, 470 (1917).

(14) R. Bentley and D. S. Bhate, *J. Biol. Chem.*, **235**, 1225 (1960).

(15) J. Nicolle and F. Weisbuch, *Compt. rend.*, **240**, 84 (1955).

(16) E. S. Lewis, *Tetrahedron*, **5**, 143 (1959).

(17) A. Streitwieser, R. H. Jagow, R. C. Fahey and S. Suzuki, *J. Am. Chem. Soc.*, **80**, 2326 (1958); R. R. Johnson and E. S. Lewis, *Proc. Chem. Soc.*, 52 (1958); W. H. Saunders, S. Asperger and D. H. Edison, *Chem. and Ind. (London)*, 1417 (1957).

TABLE IV

SECONDARY ISOTOPE EFFECT ON MUTAROTATION OF DEUTERIO-D-GLUCOSE AND D-GLUCOSE-1-*d* (COMPARED TO ORDINARY D-GLUCOSE), 25°^a

Compound	k_H/k_D			
	H ₂ O		D ₂ O	
	In neutral soln.	In acid-catalyzed reaction	In neutral soln.	In acid-catalyzed reaction
Deuterio-D-glucose	1.17 ± 0.04	1.05 ± 0.03	1.16 ± 0.01	1.09 ± 0.04
D-Glucose-1- <i>d</i>	1.12 ± 0.03	1.09 ± 0.02	1.16 ± 0.01	1.05 ± 0.04

^a The secondary deuterium isotope effect of deuterio-D-mannose in H₂O and D₂O is in the range of 1.1 to 1.2. The uncertainties in k_1 for mannose are considerably greater than those for glucose, the reaction rates being much faster. Consequently the numerical values for the secondary isotope effect for mannose are not included in Table IV.

TABLE V

RATE CONSTANTS OF MUTAROTATION OF GLUCOSE IN H₂O-D₂O MIXTURES, 25°

$$k_N = k_{0,N} + k_{1,N}(\text{HClO}_4)$$

<i>N</i>	$k_{0,N}$	$k_{1,N}$
0	0.0102	0.28
0.23	.0077	.27
.31	.0071	.26
.48	.0061	.26
.65	.0059	.22
1.0	.0029	.21

on carbon 1 or glucose, and none of the other C-D bonds have significant influence on the rate. This is a reasonable assumption, since carbon 1 is immediately adjacent to the reaction center where O-H bonds are broken and reformed during the rate-determining step. This situation is likewise quite consistent with the observations of Challis, Long and Pocker.⁶

The acid catalysis of mutarotation of glucose at 25°, in the range 0 to 0.04 *M* perchloric acid, also has been studied in H₂O-D₂O mixtures. For

a given value of *N*, where *N* is the mole fraction of D₂O in the solvent mixture, the data yield linear plots of the observed rate constants *vs.* the molarity of the acid catalyst. The results are summarized in Table V. The primary deuterium isotope effect is given by k_{H_2O}/k_N , where k_{H_2O} is the value of *k* for *N* = 0, and this increases with increase in *N*, as is expected. The failure of the Cross-Butler theory to predict the rates of acid-catalyzed mutarotation of glucose in H₂O-D₂O mixtures already has been discussed by Purlee.¹⁸

A few isolated experiments were carried out with glucose and deuterio-D-glucose in the *pH* range 7.8 to 8.45, using tris-(hydroxymethyl)-aminomethane buffers in aqueous medium. In every case, the rate constant for fully deuterated glucose is smaller than for glucose. The secondary isotope effect, k_H/k_D , for a given *pH* in this *pH* region varies from 1.1 to 1.2.

Acknowledgment.—We wish to thank Dr. Elsie Gulyas for help in making the polarimeter measurements.

(18) E. L. Purlee, *J. Am. Chem. Soc.*, **81**, 263 (1959).

[CONTRIBUTION FROM THE ROHM AND HAAS COMPANY, REDSTONE ARSENAL RESEARCH DIVISION, HUNTSVILLE, ALABAMA]

The Tetrafluorohydrazine-Difluoroamino Radical Equilibrium¹

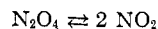
BY FREDERIC A. JOHNSON AND CHARLES B. COLBURN

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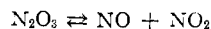
Tetrafluorohydrazine and difluoroamino radicals were found to exist in equilibrium. The enthalpy and entropy changes of this reaction were determined by two independent methods. Measurement of the pressure dependence at constant volume was used to calculate a series of K_p 's between 100 and 150°. K_f was obtained at five degree intervals in this temperature range by extrapolation of K_p to zero pressure. The enthalpy change by this method averaged 19.9 kcal./mole with no significant temperature dependence; the entropy change was 39.9 e.u. A spectrophotometric method based on the temperature dependence of the ultraviolet absorption of the difluoroamino radical gave an enthalpy change of 21.7 kcal./mole and an entropy change of 45.0 e.u.

Introduction

Only a few gaseous molecule-radical systems stable at ordinary temperatures are known. The reactions



and



are perhaps the best known examples of this type of behavior and have been studied extensively by Bodenstein,² by Verhoek and Daniels³ and by others. Another system in which a weak nitrogen-nitrogen bond is responsible for a similar molecule-

radical system is the tetrafluorohydrazine-difluoroamino radical equilibrium.

The low N-N bond strength in tetrafluorohydrazine results in the presence of detectable amounts of difluoroamino radicals even at ambient temperatures. The ultraviolet spectrum of tetrafluorohydrazine has a pressure and temperature dependent band whose maximum is at 260.2 m μ . This band is due to NF₂ radicals and observation of its variation with temperature and pressure offers a convenient means of completely characterizing the equilibrium. To check this method and to obtain data more easily at higher temperatures, the familiar measurement of pressure at constant volume allows calculation of equilibrium constants over a range of temperatures. The enthalpy

(1) This research was carried out under Army Ordnance Research Contract No. DA-01-021 ORD-5135.

(2) Bodenstein, *Z. physik. Chem.*, **100**, 68 (1922).

(3) F. Verhoek and F. Daniels, *J. Am. Chem. Soc.*, **53**, 1250 (1931).