CATALYSED REACTIONS IN ISOTOPIC WATER MIXTURES

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CONTENTS

INTRODUCTION

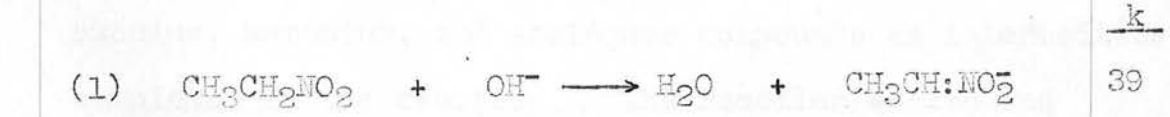
The discovery of the hydrogen isotope, deuterium, was recognised as one of the most important events in the history of physical chemistry in the last twenty years. The comparatively large differences in the physical properties of the hydrogen isotopes and their compounds led immediately to the use of deuterium as an indicator and also as a tool with which to investigate the mechanisms of reactions involving hydrogen and its compounds. The commercial preparation of deuterium oxide ('heavy water') and its availability at a comparatively low price has enabled chemists to use this isotopic water in place of ordinary water. In the field of homogeneous catalysis this has been particularly advantageous and as the following work deals with homogeneous catalysis in isotopic water solutions I append a short summary of the work hitherto done and the relevant ideas held at present.

As a general rule, in the gaseous phase, deuterium compounds react more slowly than do the corresponding hydrogen compounds but according to the kinetic theory the larger mass of the deuterium compound and hence its smaller velocity resulting in a smaller collision number is inadequate to explain the observed difference in reaction velocity. In the case of homogeneous catalysis in aqueous solution it was surprising to find that in very many cases the reaction in heavy water catalysed by D-compound proceeded considerably more rapidly than that in light water catalysed by H-compound. Both the hydrogen-ion

and hydroxyl-ion catalysed hydrolyses of esters, the acid-catalysed hydrolysis of sucrose, the iodination of acetone, and many other reactions proceed more rapidly in heavy water than in light. The mutarotation of sugars, bromination of nitromethane, and decomposition of nitramide are examples of reactions proceeding faster in light than in heavy water.

Qualitatively it is possible to explain the increased rate of catalysed reactions in heavy water by assuming that a critical intermediate complex is formed between the catalyst and the substrate. The D-complex formed in heavy water will have a lower zero-point energy than the H-complex formed in light water. Consequently the concentration of the former will be greater than that of the latter and, the reaction rate being assumed proportional to the complex concentration, the rate will be greater in heavy water than in light.

Before discussing this idea in greater detail Wynne-Jones' study of the neutralisation of the pseudo--acid nitroethane may be briefly mentioned[1]. The neutralisation process in ordinary water is shown by equation (1).

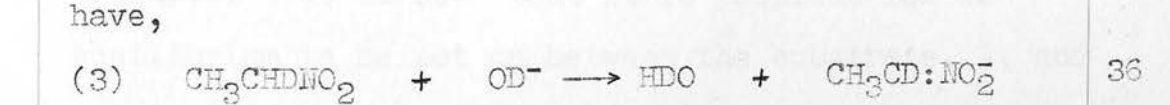


$$(1)\quad CH_3CH_2NO_2 + OH^- \longrightarrow H_2O + CH_3CH{:}NO_2^- \qquad k = 39$$

In heavy water solution and in presence of a deuteroxyl base reaction (2) takes place.

$$(2)\quad CH_3CH_2NO_2 + OD^- \longrightarrow HDO + CH_3CH{:}NO_2^- \qquad k = 60$$

For the monodeuterocompound and a deuteroxyl base we have,



$$(3)\quad CH_3CHDNO_2 + OD^- \longrightarrow HDO + CH_3CD{:}NO_2^- \qquad k = 36$$

While for the dideuterocompound we have,

$$(4)\quad CH_3CD_2NO_2 + OD^- \longrightarrow D_2O + CH_3CD{:}NO_2^- \qquad k_6$$

Velocity constants for the above reactions, shown in comparable units on the right-hand side, were obtained under the same conditions and from the values given the following conclusions can be drawn.

(a). The rate of transfer of a proton (equation (2)) is at least ten times as great as the transfer of a deuton (equation (4)) under similar conditions.

(b). The rate of proton transfer to a deuteroxyl ion in heavy water (equation (2)) is about fifty per cent greater than the rate of proton transfer to a hydroxyl ion in ordinary water (equation (1)).

These results are of great importance in elucidating mechanisms of reactions involving proton and deuton transfers.

Acid Catalysis.

Confining the discussion in the meantime to catalysis by acids it is known that in all cases the participating compounds contain oxygen, nitrogen, or double-bond carbon atoms. This results in a tendency to addition of hydrogen ions to these atoms with the formation of oxonium, ammonium, and analogous compounds as intermediate complexes in the reaction. The reaction scheme can be stated as follows,

$$R + H_3O^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} RH^+ + H_2O \xrightarrow{k_3} J + H_3O^+ \qquad (5)$$

where R is the substrate molecule and J the reaction products. It is seen that it is possible for an equilibrium to be set up between the substrate, R, and the H_3O^+ ion if the value of k_3 is low compared with

k_1 and k_2. The first step of the above reaction involves a proton or deuton transfer. It was first suggested by Wynne-Jones[2] that in reactions which are faster in light than in heavy water the rate-determining step is a proton or deuton transfer, the transfer of the former to the substrate being faster than the transfer of the latter while in the reverse case an equilibrium of the above type is set up, the concentration of the complex RD^+ being greater than that of RH^+. In the latter case the complex should be in thermodynamic equilibrium with the medium and the rate determined by the combined proton and deuton activities of the solution. The former case thus corresponds to Brönsted's definition of general acid catalysis and the latter to specific hydrogen-ion catalysis. Pedersen[3] has shown, however, that equilibrium between substrate and hydrogen ion can occur even in cases of general acid catalysis. Bonhoeffer and Reitz[4] discuss this in greater detail in a recent paper published since the present work was begun. From Reitz'[5] data on the hydrogen-ion catalysed bromination of light acetone it seems fairly evident that preequilibrium between hydrogen ion and substrate exists although this reaction is a well-established case of general catalysis. The reaction is quicker in heavy than in light water. The enolisation of acetone involves both acidic and basic catalysis as is seen from the following:-

$$CH_3.CO.CH_3 \underset{A^-}{\overset{AH}{\rightleftharpoons}} \left[CH_3COH.CH_3\right]^- \xrightarrow{B} CH_3.COH{:}CH_2$$

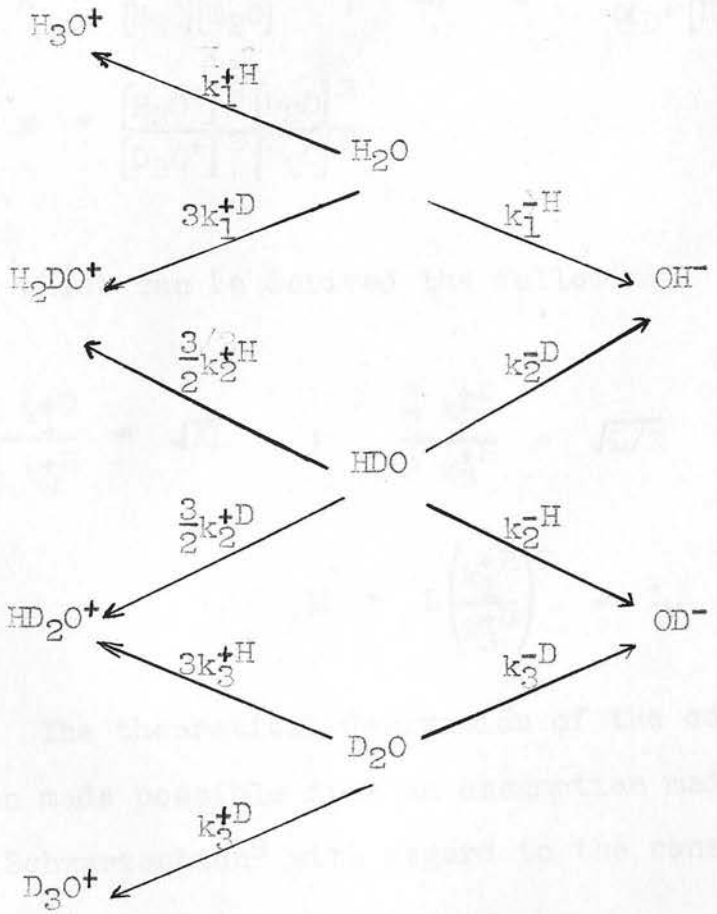
The observations indicate that equilibrium is established in the first stage but not in the second. This is confirmed by the fact that "heavy" acetone reacts more slowly than light in all media. It is clear that conclusions drawn from the relative rates in light and heavy water should be controlled whenever possible by the use of reactants containing deuterium.

The question of preequilibrium can be examined in a more quantitative way. Preequilibrium conditions in an acid-catalysed reaction hold when the rate of formation of the complex is large and is not the rate-determining step of the reaction. From the Law of Mass Action the complex concentration ought to be proportional to the hydrogen-ion activity in the solution and if the isotopic ratio D:H of the solution is varied the reaction rate will be proportional to the changes of the thermodynamic activity of the various hydrogen ions present. The variation of the combined proton and deuton activity in any solution with the D-content of the solution can be obtained empirically in various ways. La Mer and Chittum[6] by a direct conductivity method determined the dissociation constants of acetic acid at 25°C. in water-deuterium oxide mixtures. Gross and Wischin[7] examined the distribution of picric acid between benzene and isotopic water mixtures and calculated the variation of isotopic ion activity with the D-content of the water. Orr and Butler[8] using Gross' treatment but different thermodynamic constants in the

equations obtained the activity variation from the measurement of the rates of hydrolysis of acetal in formic acid- formate buffers in solutions of varying isotopic composition.

Before the activity variation can be calculated theoretically it is necessary to know something of the equilibria existing in isotopic water mixtures which are complicated systems containing three neutral molecules, H_2O, HOD, D_2O, four positive ions H_3O^+, D_3O^+, H_2DO^+, HD_2O^+, and two negative ions OD^- and OH^-.

All the possible equilibria between these species can be represented by the following constants,



where,

$$k_1^{+H} = \frac{[H_3O^+]}{\alpha_{H^+}[H_2O]} \quad ; \quad 3k_1^{+D} = \frac{[DH_2O^+]}{\alpha_{D^+}[H_2O]} \text{ etc.}$$

The symbols in brackets represent the activities of the various species while α_{H^+} and α_{D^+} are the activities of proton and deuton respectively. The difference in the k's themselves is due to the pure substitution influence while the numerical factors in front are obtained from statistical considerations. Note that in Orr and Butler's paper these factors are contained implicitly in the constants, e.g. $\frac{3}{2}k_2^{+H}$ in the above is identical with Orr and Butler's k_2^{+H}.

The proton and deuton activities may be defined by putting $k_1^{+H} = 1$, $k_3^{+D} = 1$.

Other equilibria which are known are,

1) $K = \dfrac{[HOD]^2}{[H_2O][D_2O]}$; 2) $L = \dfrac{\alpha_{H^+}[D_2O]}{\alpha_{D^+}[H_2O]}$

3) $M = \dfrac{[H_3O^+]^2[D_2O]^3}{[D_3O^+]^2[H_2O]^3}$

from which can be derived the following,

$$\frac{3\ k_1^{+D}}{\frac{3}{2}\ k_2^{+H}} = \sqrt{KL} \quad ; \quad \frac{\frac{3}{2}\ k_2^{+D}}{3\ k_3^{+H}} = \sqrt{L/K} \quad ;$$

$$M = L\left(\frac{k_1^{+H}}{k_3^{+D}}\right)^2 = L.$$

The theoretical derivation of the constants has been made possible from an assumption made recently by Schwarzenbach[9] with regard to the constants. It is equivalent to,

$$\frac{k_1^{+H}}{k_1^{+D}} = \frac{k_2^{+H}}{k_2^{+D}} = \frac{k_3^{+H}}{k_3^{+D}}$$

Using this relation we have,

$$\frac{K_3^{+H}}{K_1^{+H}} = \frac{1}{M^{1/3}} \quad ; \quad \frac{K_2^{+H}}{K_1^{+H}} = \frac{2}{M^{1/6}\,K^{1/2}}$$

At 20°C. Topley and Eyring[10] find K = 3·27.

From Korman and La Mer's measurements with the quinhydrone electrode the value of L has been found to be 15·3 at approximately 15°C.

Thus,

$$k_3^{+H} = 0{\cdot}403 \qquad \therefore \quad 3\,k_3^{+H} = 1{\cdot}209$$

$$k_2^{+H} = 0{\cdot}702 \qquad \therefore \quad \tfrac{3}{2}\,k_2^{+H} = 1{\cdot}053$$

These constants agree reasonably well with those obtained empirically by Orr and Butler[8]. They obtained

$$3\,k_3^{+H} = 1{\cdot}1 \qquad \tfrac{3}{2}\,k_2^{+H} = 1{\cdot}05$$

The total concentration of the isotopic hydrogen ions in the solution is,

$$\Sigma H_3O^+ = H_3O^+ + H_2DO^+ + HD_2O^+ + D_3O^+$$

$$= \frac{\alpha_{H^+}}{f^+}\left\{[H_2O] + \tfrac{3}{2}k_2^{+H}[HDO] + 3k_3^{+H}[D_2O] + \frac{\alpha_{D^+}}{\alpha_{H^+}}[D_2O]\right\}$$

where f^+ is the activity coefficient of the hydrogen ions.

$$\therefore \alpha_{H^+} = \frac{\Sigma H_3O^+ f^+ [H_2O]^{1/2}}{Q'(n)}$$

where,

$$Q'(n) = [H_2O]^{3/2} + [HDO][H_2O]^{1/2}\tfrac{3}{2}k_2^{+H} + [D_2O][H_2O]^{1/2}\,3k_3^{+H} + \frac{[D_2O]^{3/2}}{\sqrt{L}} \qquad (6)$$

also,

$$\alpha_{D^+} = \frac{\Sigma H_3O^+ f^+ [D_2O]^{1/2}}{Q(n)}$$

where,

$$Q(n) = Q'(n)\sqrt{L}$$

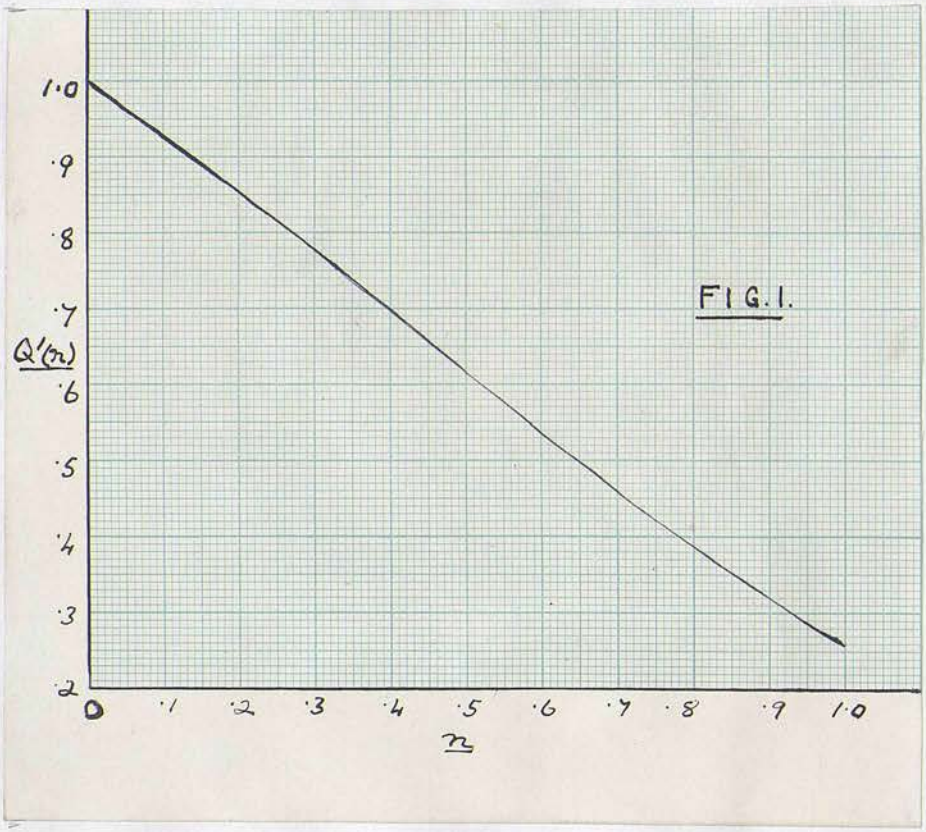


FIG. 1.

When K = 4 it has been shown that $[H_2O] = (1 - n)^2$ $[D_2O] = n^2$, $[HDO] = 2n(1 - n)$ where n is the fraction $\frac{D}{D + H}$. Since K = 3·27 here, the calculation of $[H_2O]$ etc., is not simple but the deviation from K = 4 can be allowed for and expressed by a function $\phi(n)$ such that,

$$[H_2O] = (1-n)^2 \phi^2(1-n) \quad ; \quad [D_2O] = n^2 \phi^2(n)$$

$$[HDO] = 2n\phi(n)(1-n)\phi(1-n)$$

Thus equation (6) becomes,

$$Q'(n) = \left\{(1-n)^3\phi^3(1-n) + 2n\phi(n)(1-n)^2\phi^2(1-n)\tfrac{3}{2}k_2^{+H} + n^2\phi^2(n)(1-n)\phi(1-n)3k_3^{+H} + \frac{n^3\phi^3(n)}{\sqrt{15\cdot3}}\right. \qquad (7)$$

When $\Sigma H_3O^+ = 1$ substitution in equation (7) for various values of n will give the corresponding values of Q'(n). The results are shown in Table 1.

Table 1

n	$\phi(n)$	Q'(n)
0·00	1·104	1·000
0·25	1·055	0·816
0·50	1·023	0·612
0·75	1·008	0·421
1·00	1·000	0·260

Fig. 1 shows Q'(n) plotted against n. Thus the variation of the combined proton and deuton activities with the D-content of the water is obtained.

If the rate of the reaction is assumed proportional to the proton and deuton activities we can write,

$Kn = \theta_1\alpha_{H^+} + \theta_2\alpha_{D^+}$ where Kn is the velocity constant in water of deuterium content n ; θ_1 and θ_2 are constants.

From previous equations,

$$K_n = \Sigma H_3O^+ f^+ \frac{}{Q'(n)} \left\{ \theta_1 (1-n)\phi(1-n) + \theta_2 \frac{n\phi(n)}{\sqrt{L}} \right\}$$

The rates in water and deuterium oxide respectively are, $K_0 = \theta_1 \Sigma H_3O^+ f^+$; $K_1 = \theta_2 \Sigma H_3O^+ f^+$

If $\xi_n = \frac{K_n}{K_0}$ for the ratio of the rate in a given solution to that in water at the same concentration of hydrogen ions then,

$$\xi_n = \frac{1}{Q'(n)} \left\{ (1-n)\phi(1-n) + \frac{K_1}{K_0} Q'(1)\, n\phi(n) \right\}$$

$$\therefore Q'(n) = \frac{1}{\xi_n} \left\{ (1-n)\phi(1-n) + \frac{K_1}{K_0} Q'(1)\, n\phi(n) \right\} \qquad (8)$$

Here $Q'(1) = \frac{1}{\sqrt{L}} = \cdot 26$ for $15^\circ C$.

On examination of the rates of a given reaction catalysed by acids in isotopic water mixtures the kinetic data can be substituted in equation (8). If the Q'(n) vs. n curve obtained agrees with the theoretical thermodynamic curve the assumption that the reaction rate is proportional to the proton and deuton activities is justified and preequilibrium between isotopic hydrogen ion and substrate is probably established. If the experimental curve does not agree with the thermodynamic, the assumption is not valid.

Instead of evaluating Q'(n) from the experimental values of ξ_n it is preferable to obtain theoretical values of ξ_n from the known values of Q'(n) obtained above for various isotopic compositions, and ξ_1 found from experiment. The ξ_n vs. n calculated curve can then be compared with that actually observed. Table 2 below shows the values of ξ_n calculated for different values of ξ_1.

Variation of $\xi_{(n)}$ with $\xi_{(1)}$

$\xi_{(n)}$ derived from equation, $\xi_{(n)} = \frac{1}{Q'(n)} \left\{ (1-n)\phi(1-n) + n\phi n\, Q(n)\, \xi_{(1)} \right\}$

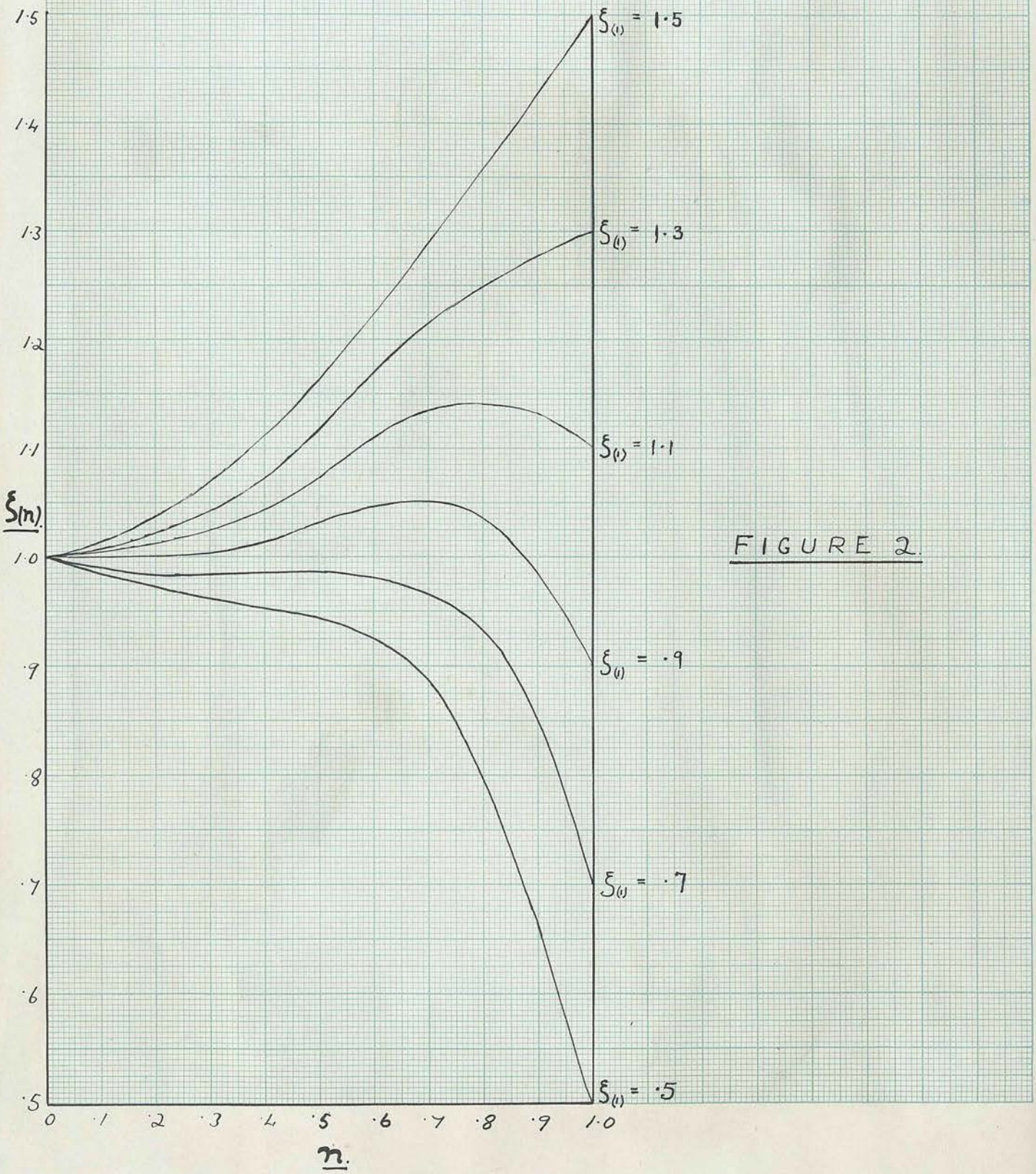


FIGURE 2.

Table 2

n	ξ_n					
	ξ_1 =1.5	ξ_1=1·3	ξ_1=1·1	ξ_1 =0·9	ξ_1=0·7	ξ_1=0·5
0·00	1·000	1·000	1·000	1·000	1·000	1·000
0·25	1·051	1·032	1·018	1·001	0·984	0·966
0·50	1·161	1·117	1·073	1·031	0·986	0·944
0·75	1·323	1·232	1·140	1·048	0·953	0·849
1·00	1·500	1·300	1·100	0·900	0·700	0·500

The various ξ_n vs. n curves obtained are shown in Fig. 2.

For the hydrolysis of acetal[8] in H(D)Cl solutions the experimental curve agrees well with the thermodynamic which is to be expected since Brönsted and Wynne-Jones[11] showed that this reaction is a case of specific hydrogen-ion catalysis. The experimental curve obtained for the decomposition of diazoacetic ester catalysed by protons and deutons[7] agrees well with the thermodynamic. Incidentally this reaction has never been considered as a case of general acid catalysis. The acid-catalysed inversion of sucrose studied by Gross and co-workers[7] shows a deviation between experimental and thermodynamic curves which seems to be outside the experimental error. Gross therefore concludes that the preequilibrium between substrate and hydrogen ion is disturbed in this case and besides the specific effect of the hydrogen ion general acid catalysis also plays a part. This view is supported by the experiments of

Hantzsch and Weissberger[12] which are discussed by Hammett and Paul[13].

Base Catalysis.

Reactions which proceed in presence of bases can be divided into two categories.

(1) Those which proceed faster in heavy water than in light e.g., most hydrolytic reactions like the hydrolysis of ethyl acetate, hydrolysis of monochloracetate etc.

(2) Those which proceed faster in light than in heavy water as the mutarotation of glucose and decomposition of nitramide.

In the case of ester hydrolysis substitution of light water by heavy in the base catalysis results in a smaller increase in the velocity than in the acid catalysis, e.g., for acid catalysis $\frac{K_{\text{IN } D_2O}}{K_{\text{IN } H_2O}} \backsimeq 1.7$ while for base catalysis $\frac{K_{\text{IN } D_2O}}{K_{\text{IN } H_2O}} \backsimeq 1.22$ under approximately the same conditions where k refers to the velocity constants in the two media.

Reitz[14] considers that although there may be hydroxyl and deuteroxyl ions present in the solution true basic catalysis may not take place. In the Brönsted sense a base is a proton acceptor and basic catalysis must always begin with a proton transfer from substrate to catalyst corresponding in acid catalysis to the addition of a proton to the substrate. The hydroxyl and deuteroxyl ions however can not only function as proton acceptors but in contrast to H_3O^+ ions they themselves can add on to the substrate and initiate the reaction in this way. From the similarity

of the constants for acid and base catalysis of esters we may conclude that the addition mechanism is probable in both cases.

The mutarotation of glucose exhibits true basic catalysis. Both for the acid catalysis and base catalysis, the catalyst in the latter case being water molecules or acetate ions, there is a decrease in reaction rate in heavy water although different mechanisms hold for the two types of catalysis. The other reactions of the second category are mostly typical prototropic reactions in which the transfer of a proton is the rate-determining step (see p.2). These reactions are thus specially suitable for comparing the rate of transfer of a proton with that of a deuton.

Experiments to find the velocity dependence of the reaction on the D-content in isotopic water mixtures have been carried out for nitramide decomposition and the water catalysed mutarotation of glucose by La Mer[15] and Hamill and La Mer[16]. Reitz has also examined the bromination of nitromethane. As in acid catalysis deviations from linearity have been encountered when k, the velocity constant of the reaction is plotted against n, the atom fraction of deuterium in the medium. A sagged curve is obtained in these cases. For nitramide and glucose the character of the curve can be accounted for by assuming that in those compounds there is one 'kinetically active' atom in the molecule which in the case of glucose is

that of the aldehydic group. Between this atom and the deuterium of the water there is an exchange set up and equilibrium is considered to be established immediately. The rate of the reaction is then governed by the ratio of the light to the heavy substrate being linear with this ratio. The bromination of nitromethane however cannot be explained by such a mechanism, as was shown by Reitz. The exchange in this case was completed by heating up the substrate with the medium before addition of bromine. The proportion of heavy compound could be calculated but the rate of bromination was not found to be linear with this ratio.

The variation of the activities of the hydroxyl and deuteroxyl ions with the composition of the water could be established by determination of the dissociation constants of a weak base, or alternatively, by calculation from the constants given above for the acid catalysis, i.e., k_1^{+H}, L, M, etc., together with the dissociation constants of light and heavy water. Since these constants account successfully for the course of the hydrogen ion catalysis, the latter course has been adopted. The relative concentrations of hydroxyl and deuteroxyl ions are determined by the equation,

$$2\,OD^- + H_2O \rightleftharpoons 2\,OH^- + D_2O$$

Writing,

$$N = \frac{[OH^-]^2[D_2O]}{[OD^-]^2[H_2O]}$$

and,

$$k_1^{-H} = \frac{[OH^-]\alpha_{H^+}}{[H_2O]} \quad ; \quad k_3^{-D} = \frac{[OD^-]\alpha_{D^+}}{[D_2O]}$$ see p. 6,

we have from previously known constants,

$$N = \frac{1}{M}\left(\frac{k_1^{+H}.k_1^{-H}}{k_3^{+D}.k_3^{-D}}\right)^2 = \frac{1}{M}\left(\frac{K_{H_2O}}{K_{D_2O}}\right)^2$$

where $K_{H_2O} = [H_3O^+][OH^-]$ and $K_{D_2O} = [D_3O^+][OD^-]$

i.e., the ionic products of light and heavy water.

From the data of Wynne-Jones,[18]

$$\frac{K_{D_2O}}{K_{H_2O}} = 0{\cdot}184 \text{ at } 15^oC. \quad \therefore N = 1{\cdot}93.$$

Now $$\frac{[OD^-]}{[OH^-]} = \sqrt{\frac{[D_2O]}{N[H_2O]}} = R(n) \text{ say.}$$

If the total concentration of hydroxyl ions in the solution is, ΣOH^-,

$$\therefore \Sigma OH^- = [OH^-] + [OD^-]$$

$$[OH^-] = \frac{\Sigma OH^-}{1 + R(n)} \quad \text{and,}$$

$$[OD^-] = \frac{\Sigma OH^-}{1 + 1/R(n)}$$

Therefore if the rate of the reaction is determined by the activities of the hydroxyl and deuteroxyl ions we have,

$K_n = k_1[OH^-] + k_2[OD^-]$ where K_n is the velocity constant in water of deuterium content n.

$$\therefore K_n = \Sigma OH^-\left\{\frac{k_1 + k_2R(n)}{1 + R(n)}\right\}$$

The rates in water and deuterium oxide respectively are, $K_o = k_1\Sigma OH^-$ and $K_1 = k_2\Sigma OH^-$

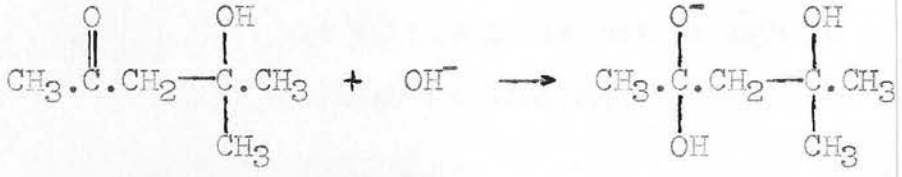
$$\therefore \frac{k_2}{k_1} = \frac{K_1}{K_o} = \xi_{(1)} \qquad \text{if } \Sigma OH^- \text{ is kept constant.}$$

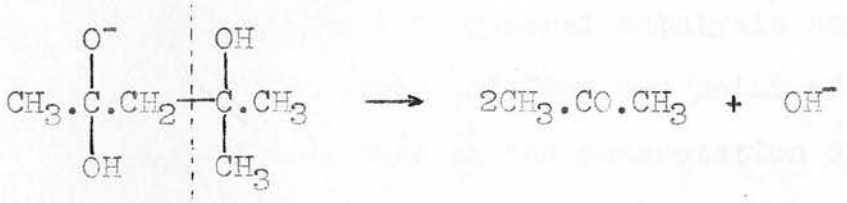
$$\frac{K_n}{K_o} = \xi_{(n)} = \left\{\frac{1 + \xi_{(1)}R(n)}{1 + R(n)}\right\} \qquad (9)$$

$\xi_{(n)}$ is the ratio of the rate in a given solution to that in water at the same concentration of hydroxyl ions. If $\xi_{(1)}$ is known for any reaction catalysed by the ions -OH and -OD the theoretical values for the rates at any D-content of the solution can be calculated from equation (9) the assumption being that the rate is proportional to the combined activities of the two ions. Comparison of the actually observed rates with the theoretical rates will show whether or not the aforementioned assumption is justified.

The decomposition of diacetonealcohol to form two molecules of acetone has been examined by Hornel[19] who found $\frac{K_1}{K_o} = 1{\cdot}22$ at 15°C. Although little is known of the mechanism of this reaction there are two possibilities which may be represented as follows,

1)

(a) 

(b) 

In (a) a complex is formed by addition of the -OH group which complex then splits up as in (b) to form ultimately two molecules of acetone.

2)

(a) 

(b) 

In (a) the hydroxyl ion of the base removes a hydrogen ion from one of the two terminal methyl groups of the alcohol. The negative charge on the complex tends to weaken the bond between carbon atom 1 and 2 resulting in the complex splitting up as in (b).

According to the latter scheme the difference between the reaction rate in heavy and light water must be due to the difference in the rates of removal of a proton by -OD and -OH respectively. Wynne-Jones has already shown (see p. 2) that the transfer of a proton to a deuteroxyl base in heavy water is about fifty per cent greater than the transfer to a hydroxyl base in light water. The experimental data thus supports the second mechanism but this in itself is not enough to prove either one or the other mechanism.

General Acid and Base Catalysis

Only a few reactions subject to general catalysis have been studied in isotopic water and from our point of view the most interesting case is the mutarotation of glucose. This reaction was examined by Moelwyn-Hughes and Bonhoeffer[20] who compared the catalytic activity of D_3O^+ ions with that of H_3O^+ ions in the mutarotation. These authors found the ratio $k_{D_3O^+}/k_{H_3O^+}$ to be ·561

at 14·80°C. and to increase with temperature. The result is interesting since this is the only case of an acid-catalysed reaction hitherto studied which shows a decrease in velocity in heavy water. The solvent molecules are also catalysts in the reaction but the effect of those have been taken into account, the values being known from the data of Moelwyn-Hughes, Klar and Bonhoeffer[21]. A more thorough investigation of the mutarotation was carried out by Hamill and La Mer[16] who ascertained the effect of the D-content of the solution on the catalysis by the acid ion, the aqueous molecules, an anion base and the conjugate molecular acid. Two results of importance appear.

1) The velocity of the water-catalysed reaction does not vary linearly with the D-content but with the fraction of 'heavy' glucose present calculated from the following equation,

$$k_{obs.} = k_{oH_2O} - (k_{oH_2O} - k_{oD_2O})F_{DG} \qquad (10)$$

Here $k_{oD_2O} = 55\, k_{D_2O}$; $k_{oH_2O} = 55\, k_{H_2O}$

$$F_{DG} = \frac{DG}{DG + HG} = \text{fraction of heavy glucose.}$$

Also $\frac{DG}{HG} = \frac{F_{DG}}{(1 - F_{DG})}$ and $K_g = \frac{[DG][H_2O]}{[HG][HDO]}$

Let K_t = exchange constant for tetramethylglucose. This possesses only one exchangeable hydrogen atom which is on the aldehydic group. The constant was found experimentally to be equal to 0·84.

The above conclusion was reached by firstly assuming that equation (10) held for the mutarotation process. The F_{DG} thus calculated was used with the help of the above relations to find K_g, the exchange constant between light and heavy glucose. The value of K_g for each kinetic measurement remained constant and agreed excellently with the K_t for tetramethylglucose found from other experiments, i.e., 0·84. This justifies the above assumption that the reaction rate is directly proportional to the fraction of heavy glucose present which arises from exchange of the kinetically active hydrogen of the aldehydic group with the heavy water.

2) The velocity of the acid-ion catalysis varies linearly with the D_2O-content of the solvent. The data actually fits the equation,

$$k_{H^+D^+} = 0{\cdot}311 - 0{\cdot}084\, F_{D_2O}.$$

F_{D_2O} = fraction of D_2O in the solvent.

The authors conclude that in 2) there is unlikely to be any real dependence of $k_{H^+D^+}$ on the D_2O-content of the medium since its composition is very complex.

The objects of the work described in this thesis were briefly as follows.

(1) To examine the acid-catalysed hydrolyses of the simple esters ethyl formate and methyl acetate in mixtures of light and heavy water of varying isotopic composition and to ascertain whether the reaction rate

was governed by preequilibrium conditions.

(2) To elucidate as far as possible the mechanism of the decomposition of diacetonealcohol in alkaline solutions. To this end the decomposition of 'light' diacetonealcohol in alkaline solutions of varying D-content but constant alkalinity was observed. The alkaline decomposition of 'heavy' diacetonealcohol in light and heavy water was also examined.

(3) To examine a known case of general catalysis, i.e., the mutarotation of α-d-galactose and obtain the effect of the hydrogen ions in water of varying isotopic composition. The kinetic and theoretical thermodynamic curves for catalysis by the hydrogen ions could then be compared.

Incidentally the catalytic constants for the ions -OH and -OD in the mutarotation were obtained.

EXPERIMENTAL AND RESULTS

Methods of following the reactions.

On account of the small volumes dealt with in the heavy water experiments a physical method of following the reaction was preferred to a chemical one but only in cases of reactions where the change of physical property was large enough could this method be used. In the case of hydrolysis of ethyl formate and decomposition of diacetonealcohol the refractive index change was fairly large and could be followed in an interferometer.

(1) Interferometric Method.

A Hilger Rayleigh interferometer having a high-grade one cm. cell was used. During the experiment the cell was kept in a metal chamber with windows cut in the ends thus allowing the light from the source to pass through each of the two compartments of the cell. The chamber was water-jacketed and a circulating pump maintained a constant flow of water at 15°C. through the jacket. The water was drawn from a thermostat electrically controlled to give a temperature of 15± .05°C. allowance being made for a rise or drop of temperature outside the thermostat according to the air temperature of the surroundings. The cell itself consisted of two compartments whose capacity was each two ml. In the experiments with ethyl formate it was found convenient to have one compartment very nearly filled

up with the reaction mixture while for diacetone-alcohol about one ml. reaction solution was sufficient to give good end-points. The other compartment of the cell was filled with a reference solution of convenient refractive index such that the index change could be followed on the interferometer scale.

Two different methods were adopted in initiating the reaction.

(a) Ethyl Formate.

To approximately two ml. of the H(D)Cl mixture in a specimen tube previously cooled in the thermostat to 15°C. was added ·15 ml. of the ester from a calibrated syringe. The time of this addition was noted and taken as the starting point of the reaction. The contents of the tube were thoroughly and quickly mixed and about two ml. of the mixture introduced into the cell compartment. Thereafter interferometer readings and times were taken. After a sufficient time had elapsed (about twelve times the half-time period of the reaction was considered as sufficient) the end-reading of the reaction was taken. In some cases a drift of the end-reading was observed and regarded as evidence of evaporation from the cell contents. This evaporation was reflected in the kinetic curves obtained and recourse was had to an indirect method for calculating the end-point.

(b) Diacetonealcohol.

One ml. of the NaOH(D) solution was introduced into one side of the cell the reference solution being on the other. The cell was allowed to attain a temperature of 15°C. by cooling for about one hour at the end of which ·025 ml. of the alcohol previously cooled to 15°C. was introduced from a calibrated syringe. This was taken as the start of the reaction. After shaking the cell thoroughly, good fringes were obtained in a few minutes and readings and corresponding times were noted.

Conditions for obtaining the velocity constants were very much better in the case of diacetonealcohol. One advantage was the fact that for the quantities used a shift of 250 drum divisions was obtained throughout the reaction while for ethyl formate a shift of only about 35 drum divisions was recorded. The greater shift in the first case allows more readings to be obtained and the end-point can be fixed more accurately. In any case owing to the smaller amount of substrate added the evaporation of the products is reduced resulting in increased accuracy when fixing the end-point.

The hydrolysis of a simple ester may be considered a monomolecular reaction provided as in the above case the concentration of the ester is small. The decomposition of diacetonealcohol is also kinetically of the first order. The velocity constants of these reactions were obtained by plotting,

$\log_{10}(n_t - n_\infty)$ vs. t and evaluating the slope of the straight line obtained.

n_t = interferometer reading at time t after the start of the reaction.

n_∞ = interferometer reading at the end of the reaction.

For reactions where no stable end-reading could be observed the end-point was obtained by plotting $\frac{d}{dt}(n_t)$ against n_t and extrapolating to zero slope i.e., the n_t when $\frac{d}{dt}(n_t) = 0$.

The units of the constants were in all cases gram-moles and minutes.

The change of refractive index on hydrolysis of methyl acetate was not great enough to allow the reaction to be followed in the interferometer but a semi-micro titration method was found suitable.

(2) Titration Method.

Approximately 5 ml. of the H(D)Cl mixture was used in the reaction. After cooling both acid and ester for about 15 minutes in the thermostat about ·25 ml. of the latter was added to 5 ml. acid by means of a calibrated syringe. After thorough mixing of the solution $\frac{1}{2}$ ml. of the mixture was quickly withdrawn and run into a large excess of distilled water in a conical flask which with its contents had been previously cooled in ice. The time was now observed and the acid mixture quickly titrated with weak standard baryta-water. The initial titre was thus obtained. Half ml. portions of the reaction mixture

were withdrawn at convenient intervals and the titre obtained. The end-titration was obtained after the lapse of a convenient time up to forty-eight hours. The velocity constant, k, of the reaction was obtained from the equation,

$$k = \frac{2.303}{t_n}\left[\log_{10}(T_\infty - T_0) - \log_{10}(T_\infty - T_n)\right]$$

where,

T_∞ = titre at end of reaction.

T_0 = " " start " "

T_n = " " time t_n minutes after start of reaction.

Five intermediate titres were obtained in each reaction each titre giving a value of k when appropriate substitution was made in the equation. The five values, omitting obvious anomalies, were averaged to obtain the final velocity constant of the reaction.

(3) Polarimetric Method.

The mutarotation of α-d-galactose was observed in a Schmidt and Haensch polarimeter reading to 0.01°. Since the change of specific rotation in the change of α-d-galactose to the equilibrium mixture of the α and β forms is fairly large viz., $\Delta[\alpha]_D^{12.5} = 60^\circ$ for $\alpha \longrightarrow \alpha + \beta$ a solution containing a small concentration of the sugar, about two per cent, was used. A narrow-bore two decimetre polarimeter tube containing about two ml. of the solution was found convenient. The latter was surrounded by a water jacket through which

water from a thermostat at 15°C. was circulated before and during the experiment. The solution and a known weight of the galactose were cooled separately for about 15 minutes in the thermostat. A known volume, about 2·3 ml., of the solution was then introduced into the tube containing the sugar and the mixture thoroughly shaken for about three minutes. The polarimeter tube was filled with the reaction mixture using a thin capillary which reached to the bottom. Rotations and corresponding times were thereafter observed. The reaction is of the first order and so the velocity constant could be obtained graphically by plotting $\log_{10} (\alpha_t - \alpha_\infty)$ against t and obtaining the slope of the straight line.

α_t = rotation observed at time t minutes after start of reaction.

α_∞ = rotation on completion of reaction.

Very good linear graphs were obtained and the velocity constant was reproducible to a high accuracy. The change of rotation throughout the reaction was in all cases about 2·20°.

Treatment of Heavy Water.

The heavy water samples were obtained from Messrs. I.C.I. Ltd. and had a composition varying from 99·55 - 99·60 gm. pure D_2O per 100 gm. of sample. The density, d_4^{20} varied from 1·10490 to 1·10495. On testing the samples with B.D.H. universal indicator an alkaline reaction was invariably given, showing a pH between eight and nine. Consequently in those experiments where this amount of alkali might affect

the reaction rate e.g., when using dilute solutions of acids or bases, the heavy water sample was distilled under atmospheric pressure in an all-Pyrex distilling apparatus suitably designed for dealing with small quantities about five to eight ml. The distillate had a reaction which indicated a pH of about seven.

After distillation the density of the sample at 25°C. was measured using a pyknometer holding about one half ml. when filled to the mark. The D_2O-content of the sample was calculated from the figure denoting the specific gravity of 100% D_2O i.e., $d_{25}^{25} = 1{\cdot}1074$. In no case was the lowering of the D_2O-content of the original sample more than ·4%.

Experiments with Ethyl Formate.

Purification.

The commercial product was twice distilled, the fraction boiling at 53·85 - 54·45°C. under 760·5 mm. pressure of mercury being used in the experiments.

Preparation of Solutions.

A small quantity of concentrated hydrochloric acid solution previously standardised by means of anhydrous sodium carbonate was added to a weighed quantity of heavy water. Knowing all the weights and volumes involved the normality of the resulting solution could be calculated. The resulting decrease in the D_2O concentration of the solution was also computed. A hydrochloric acid solution in ordinary water was made up to exactly the same strength. By mixing together varying weighed quantities of each solution, mixtures of varying D-content were obtained although the total acidity of the solution was kept constant.

Results.

Normality of H(D)Cl solutions = ·201 N.

Approximately 2 ml. acid solution + ·15 ml. ester on one side of the cell; ·201 N HCl on the other.

Temperature = 15±·05°C.

FIG 3.

ETHYL FORMATE.

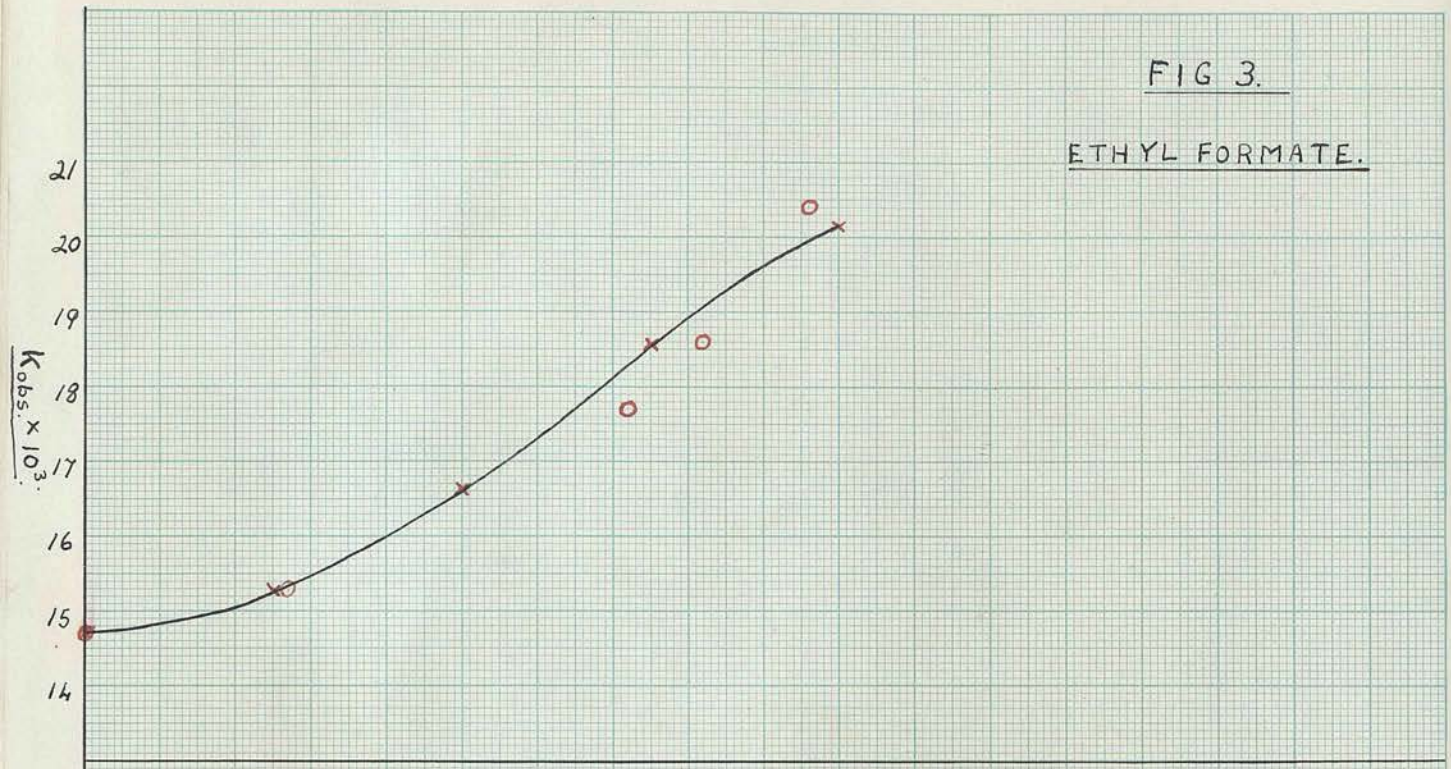


FIG 4.

METHYL ACETATE.

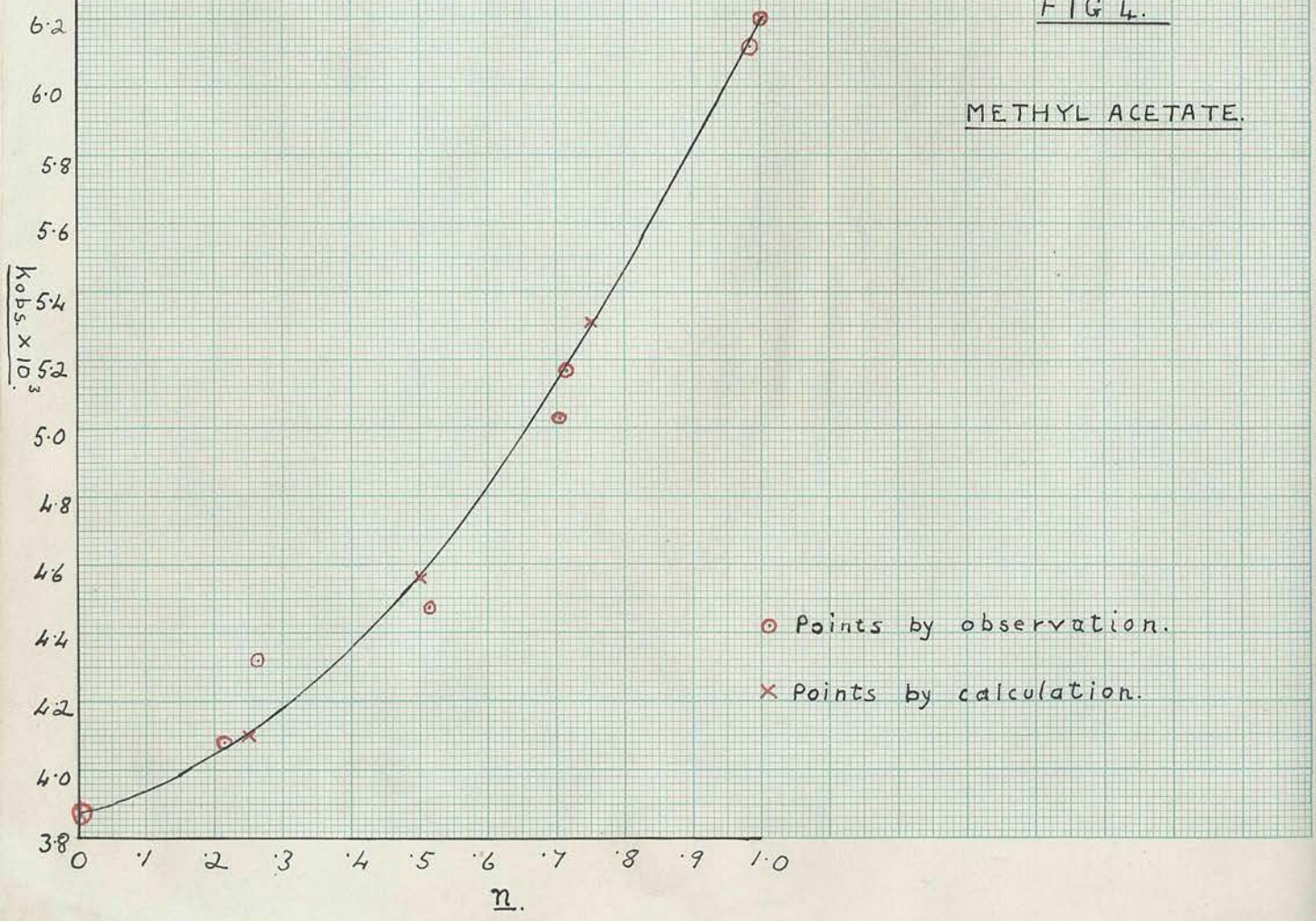


Table 3

Atom fraction D in solvent = $\frac{D}{D + H}$ = n	Observed velocity constant. $k_{obs.} \times 10^3$
·00	14·7, 15·1. Best value = 14.7
·27	15·3
·72	17·7
·82	18·6
·96	20·4
1·00	20·15 Value obtained by extrapolation from theoretical curve

The ratio of the velocity of hydrolysis in heavy water to the velocity in light water,

$$\frac{k_{obs.D_3O^+}}{k_{obs.H_3O^+}} = \frac{k_{D_3O^+}}{k_{H_3O^+}} = 1{\cdot}37.$$

The above data is also shown in Fig. 3.

Experiments with Methyl Acetate.

Purification.

Commercial methyl acetate was fractionated. The fraction of B.P. 57·0 - 57·2°C. at 759·6 mm. was collected and found to be quite neutral to B.D.H. universal indicator, showing a pH of 7 - 8.

Preparation of Solutions.

To prepare DCl solution dry hydrochloric acid gas was absorbed in heavy water, the approximate concentration being estimated from the increase in

weight of the solution. The absorption was discontinued after a convenient increase in weight was observed and the density of the resulting solution measured. Small known weights of the solution were then titrated against weak standard baryta-water and the normality of the DCl solution calculated.

A hydrochloric acid solution of the same strength as the DCl solution was prepared by diluting standard hydrochloric acid with a requisite amount of distilled water. The standardisation of the solution was carried out in the same way as for DCl solution.

As before mixtures of HCl and DCl were made up by weighing out the two solutions in varying proportions. Knowing the weights, densities and concentrations of the two solutions the D-content was calculated.

Results.

Normality of H(D)Cl solutions = 1·317 N.

5 ml. acid mixture + ·25 ml. ester mixed and ·5 ml. reaction mixture taken for each titration.

Temperature = $15 \pm ·05^{\circ}C$.

Solution 1. 1·317 N DCl. n = ·983.

$T_\infty - T_n$	t_n	$k_{obs.}\ 10^3$	Average $k_{obs.} \times 10^3$ omitting first value
11·00	00·0		
8·37	38·0	7·20	
6.84	75·5	6·29	
4·36	146·0	6·34	6·22
3·13	206·5	6·09	
1·59	315·0	6.14	

Solution 2. 1·317 N HCl. n = ·000.

$T_\infty - T_n$	t_n	$k_{obs.} \times 10^3$	Average $k_{obs.} \times 10^3$, omitting second value.
10·93	00·0		
9.72	32·5	3·61	
8·37	68·5	3·90	
6·67	138·0	3·58	3.64
5·22	200·0	3·70	
3.52	308.5	3·67	

The k's have been calculated from the equation,

$$k = \frac{2\cdot303}{t_n}\left[\log_{10}(T_\infty - T_0) - \log_{10}(T_\infty - T_n)\right]$$

The above table shows that the average deviation of each individual k from the arithmetic mean is about (1·5-2)% which represents the limit of accuracy of the experiment. The complete set of results has been tabulated below in Table 4.

Table 4

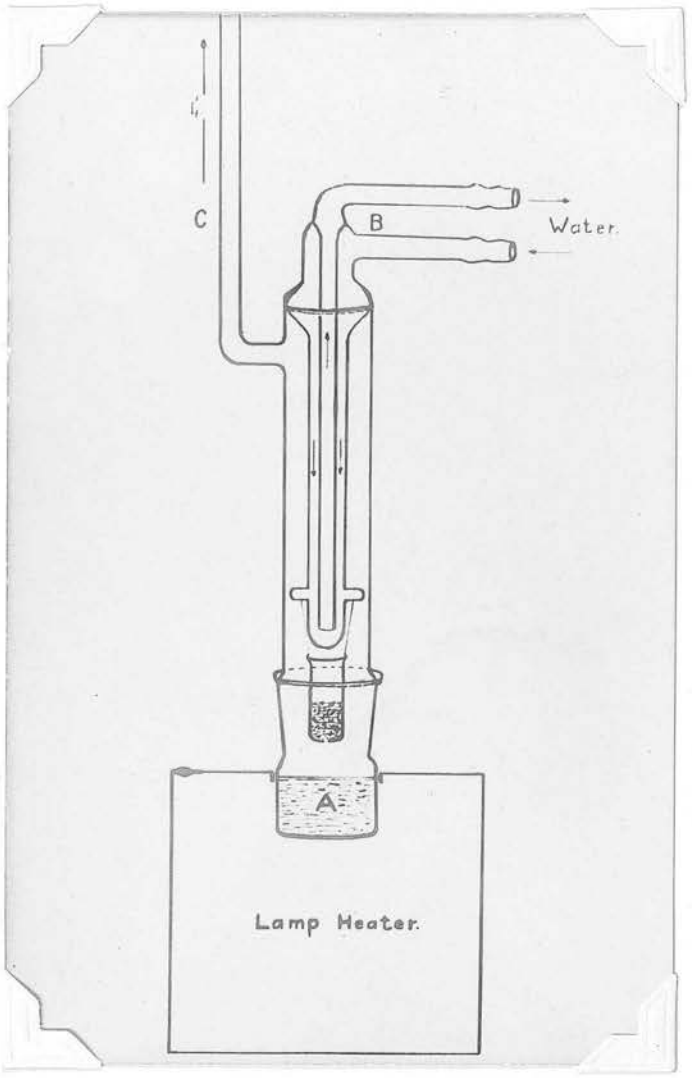
Atom fraction D in solvent = $\frac{D.}{D+H}$	Observed velocity constant $k_{obs.} \times 10^3$
·000	3·64, 3·65, 3·85, 3·89, 4·02, 4·15. Average = 3·87.
·214	4·08
·265	4·32
·512	4·47
·703	5·03
·713	5.17
·984	6·22, 6·02. Average = 6·12
1·000	6·20. By extrapolation.

In the case of the hydrolysis in hydrochloric acid the average deviation from the mean is 3·9%.

With D-content as abscissae and velocity constants as ordinates the above results are shown in Fig. 4.

In this reaction $\frac{k_{D_3O^+}}{k_{H_3O^+}} = 1{\cdot}60$,

where $k_{D_3O^+}$ and $k_{H_3O^+}$ denote the catalytic constants of the oxonium ions.


C
B
Water.
A
Lamp Heater.

Experiments with Diacetonealcohol.

Purification of ordinary compound.

Commercial diacetonealcohol, which had turned a slightly yellow colour from polymerisation on standing, was distilled under reduced pressure. A fraction of boiling point 63-64°C. at 11 mm. mercury was taken.

Preparation of 'Heavy' Diacetonealcohol.

The compound was prepared by the condensation of 'heavy' acetone. To obtain this, pure acetone was heated with approximately 100% D_2O and a trace of caustic soda in a bomb at (60-65)°C. for a few days. The resulting acetone was distilled and submitted to the same treatment with fresh heavy water. After distillation the product was estimated to have about 75% of its H atoms replaced by D, i.e., 75% atom-D. For the condensation of the acetone the method of Conant and Tuttle[22] was used and adapted to a small scale. The apparatus, of which a sketch is given on the opposite page, consisted of a semi-micro extractor made of Pyrex glass with an electrically heated cup, A, holding about 5 ml. acetone, and a condenser, B, to the bottom of which is attached a small thimble containing solid baryta, in this case heavy baryta obtained by treating ordinary baryta once with heavy water. C is a reflux for the unconverted acetone. After heating for forty-eight hours at about 100°C. the product consisting of an 80% yield of the alcohol was distilled at atmospheric

pressure and then twice distilled in vacuo. A micro-analysis carried out by Dr. C.L. Wilson of London University showed that the diacetonealcohol, assuming it was quite pure, contained $60 \cdot 4 \pm 0 \cdot 1$ atom%-D.

Preparation of Solutions.

The heavy water used for the alkaline solution was distilled before use. This rendered it both neutral and gas-free. A.R. sodium hydroxide in pellet form was then added to a requisite amount of D_2O to make an approximately decinormal solution, the process being carried out in a dry, carbon dioxide-free box. After dissolving, the sodium deuteroxide solution was standardised by means of weak hydrochloric acid, great care being taken to exclude carbon dioxide from the solutions. A sodium hydroxide solution of exactly the same concentration was made up in a similar manner using larger quantities of material. Carbon dioxide-free distilled water was used here. The reduction in the D_2O-content of the water on addition of the solid sodium hydroxide did not amount to more than ·2 per cent. The solutions of varying D-content were made up as before by weighing out and mixing varying quantities of the NaOH and NaOD solutions, the calculated D-content being checked by noting the change of refractive index produced when these solutions were introduced into the interferometer cell before the addition of the alcohol.

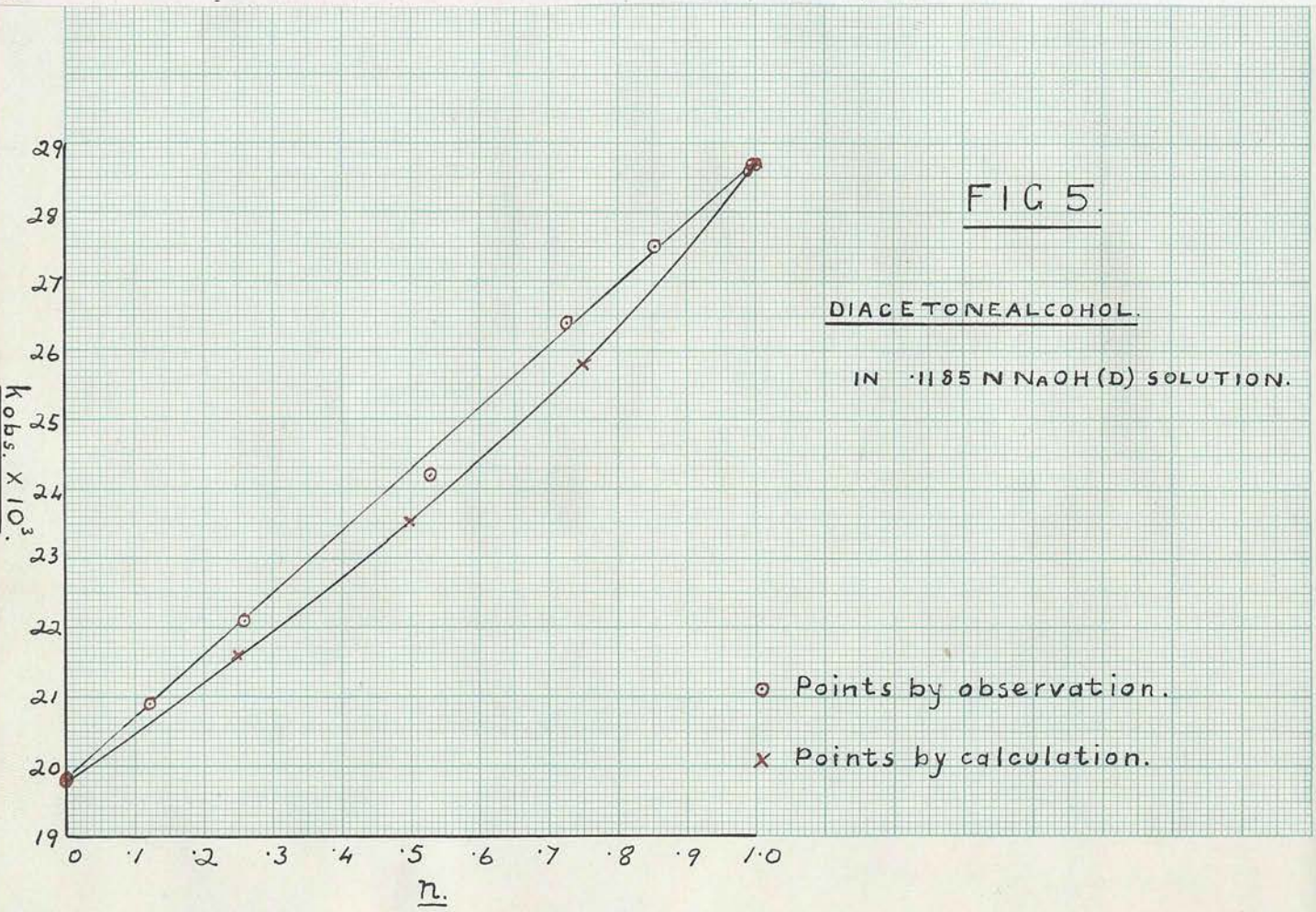


FIG 5.

DIACETONEALCOHOL.

IN ·1185 N NaOH (D) SOLUTION.

Results.

Normality of NaOH(D) solutions = ·1185 N.

1 ml. solution + ·029 ml. diacetonealcohol on one side of the cell; reference solution on the other.

Temperature of cell = 15± ·05°C.

Table 5.

Atom fraction D in solvent = n.	Observed velocity constant. $k_{obs.} \times 10^3$
0·000	19·6, 19·6, 20·4, Aver. = 19·8
0·121	20·9
0·259	22·1
0·529	24·2
0·725	26·4
0·853	27·5
0·990	28·8, 28·4, Aver. = 28·6
0·996	28·7
1·000	28·7 By extrapolation.

$$\frac{k_{OD^-}}{k_{OH^-}} = \zeta_{(1)} = 1.45$$

The above data is shown in Fig. 5.

Comparison of Velocity Constants for 'Light' and 'Heavy' Diacetonealcohol.

Table 6.

	$k_{obs.} \times 10^3$	
	0·1185 N NaOH n = ·990	0·1166 N NaOD n = ·995
'Light' diacetonealcohol	19·8	29·2
'Heavy' " (60·4 atom%-D)	15·8, (17·0*)	26·6

* Original product prior to distillation.

For ·1185 N NaOH,

$$\frac{k_{obs.} \text{ for 'light' compound}}{\text{" " 'heavy' "}} = \frac{19·8}{15·8} = \underline{1·25}.$$

For ·1166 N NaOD,

$$\frac{k_{obs.} \text{ for 'light' compound}}{\text{" " 'heavy' "}} = \frac{29·2}{26·6} = \underline{1·10}.$$

These ratios refer to a 'heavy' compound containing only 60·4 atom%-D. Assuming that, for a given medium, the decrease in reaction rate is more or less linearly proportional to the atom%-D in the diacetonealcohol we have for diacetonealcohol containing 100% atoms-D, in ·1185 N NaOH,

$$\frac{k_{obs.} \text{ for 'light' compound}}{\text{" " 'heavy' "}} \frown \underline{1·68}.$$

and in ·1166 N NaOD,

$$\frac{k_{obs.} \text{ for 'light' compound}}{\text{" " 'heavy' "}} \frown \underline{1·22}.$$

Experiments with α-d-galactose.

The pure commercial product, which was found to be practically neutral to B.D.H. indicator was used in these experiments.

Preparation of Solutions.

The method of preparing the HCl and DCl solutions was the same as in the methyl acetate experiments, the heavy water being distilled before use in this case. The solutions used in attempting to find the water rate of the reaction were obtained by diluting weak hydrochloric acid solution with a large volume of distilled water. The pH of the resulting solution was then found colorimetrically. The ordinary water phosphate buffer solution was prepared by adding the requisite amount of the A.R. salts to distilled water while for the heavy water buffer a small quantity of concentrated H_2O buffer was diluted with D_2O. The reduction of the D-content of the latter solution by the H_2O present was neglected since it did not amount to more than 1%.

Results.

Normality of H(D)Cl solutions = ·01077 N.

2·357 ml. acid solution + ·0471 gm. galactose were mixed and dissolved for each experiment.

Temperature = $15 \pm .05^{\circ}C.$

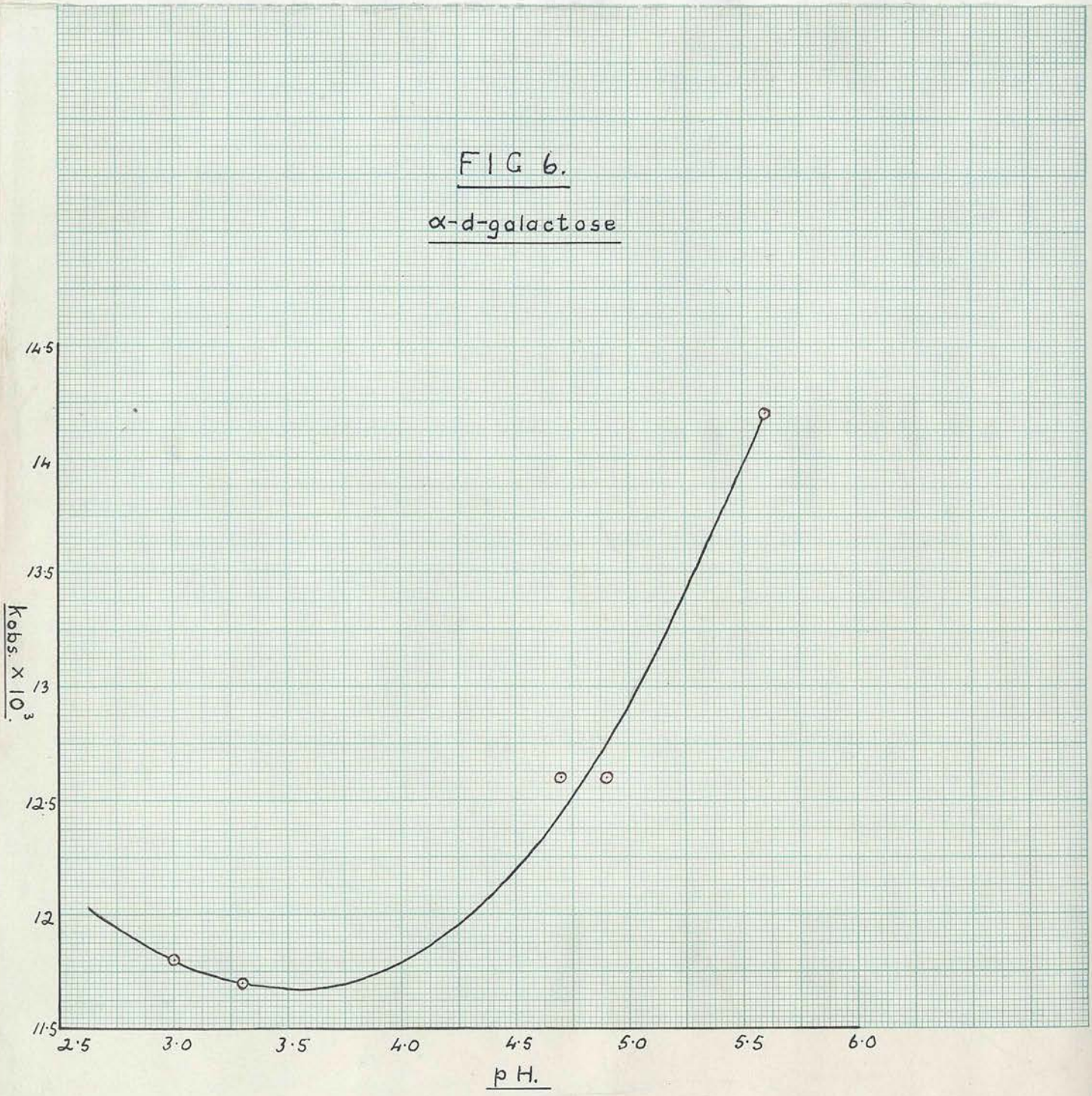
Table 7

Ratio $\frac{D}{D+H}$ in solvent	Observed Mutarotation velocity constant. $k_{obs.} \times 10^3$
·000	17·3, 17·4. Aver. value = 17·35
·247	13·49
·349	13·49
·485	11·10
·754	9·34
·995	7·40, 7·42 Aver. value = 7·41
1·000	7·40 By extrapolation

Since the mutarotation of galactose shows multiple catalysis, to find the constants for the various hydrogen ions it was necessary to find the catalytic constant for the isotopic water molecules. Kuhn and Jacob[23] show that, from experiments carried out in ·1 N citrate buffers and 5 per cent. sugar solutions, the catalytic minimum of the pH-mutarotation velocity curve occurs at pH = 3·5 where $k \times 10^4 = 15·4$ at 25°C. At the minimum which is rather sharp the catalysis should be due entirely to water molecules the ions of water having a negligible effect. On the other hand for d-glucose Nelson and Beegle[24] show that between pH = 2·5 and pH = 6·5 there is a broad catalytic minimum, the mutarotation velocity in this region being independent of the hydrogen-ion concentration.

FIG 6.

α-d-galactose



Consequently experiments were carried out with galactose to ascertain whether this broad minimum existed. The experiments were carried out in unbuffered solutions as otherwise the pure water rate could not be determined. The determination of the pH therefore was roughly made as all that was required was reproducibility of the velocity constant within a certain pH range. The results are shown in Table 8 and Fig. 6.

Table 8

Solution	pH	$k_{obs.} \times 10^3$
Conductivity water	-	14·3
Very dil. HCl solution	5·6	14·2
" " " "	4·7	12·6
·5 N H_3BO_3 "	4·9 Calculated from dissociation constant	12·6
·00055 N HCl "	3·3	11·7
·0011 " " "	3·0	11·8

The results indicate that a fairly sharp minimum occurs between pH 3 and 4 on the pH-mutarotation velocity curve, the corresponding velocity being about 11·7. The idea of obtaining the velocity constants in isotopic water mixtures directly had therefore to be given up as no control could be put on the hydrogen-ion concentration in such solutions without using buffer mixtures which would introduce other complications.

However an indirect method of calculating the water constant was available. The effect of the different ions and water molecules on the reaction rate can be put in the form of an equation first proposed by Hudson (1907).

$$k_{obs.} = C_{H_2O} \cdot k_{H_2O} + [H_3O^+]\, k_{H_3O^+} + [OH^-]\, k_{OH^-}$$

where C_{H_2O} = molar concentration of water which in dilute solutions remains practically constant.

If experiments are carried out at two different acid concentrations the following equations arise,

$$k_{1obs.} = C_{D_2O,H_2O_1} k_{D_2O,H_2O} + [H_3O^+ + D_3O^+]_1 k_{H_3O^+D_3O^+} + [OH^- + OD^-]_1 k_{OH^-OD^-} \quad (11)$$

$$k_{2obs.} = C_{H_2O,D_2O_2} k_{H_2O,D_2O} + [H_3O^+ + D_3O^+]_2 k_{H_3O^+D_3O^+} + [OH^- + OD^-]_2 k_{OH^-OD^-} \quad (12)$$

where $k_{1obs.}$ and $k_{2obs.}$ are the observed constants of mutarotation in the two solutions of different acid concentration but the same D-content.

Since the first term on the right-hand side of equations (11) and (12) keeps practically constant in dilute solutions, and in acid solutions the final term of each can be neglected, the isotopic ion constant for a given D-content is easily obtained from the equation,

$$k_{H_3O^+D_3O^+} = \frac{k_{1obs.} - k_{2obs.}}{[H_3O^+ + D_3O^+]_1 - [H_3O^+ + D_3O^+]_2}$$

The right-hand side can be evaluated from the known data. Knowing the $k_{H_3O^+D_3O^+}$ for any D-content of the solvent the water constant, k_{H_2O,D_2O}, for this content can easily be found by substitution in equation (11) or (12).

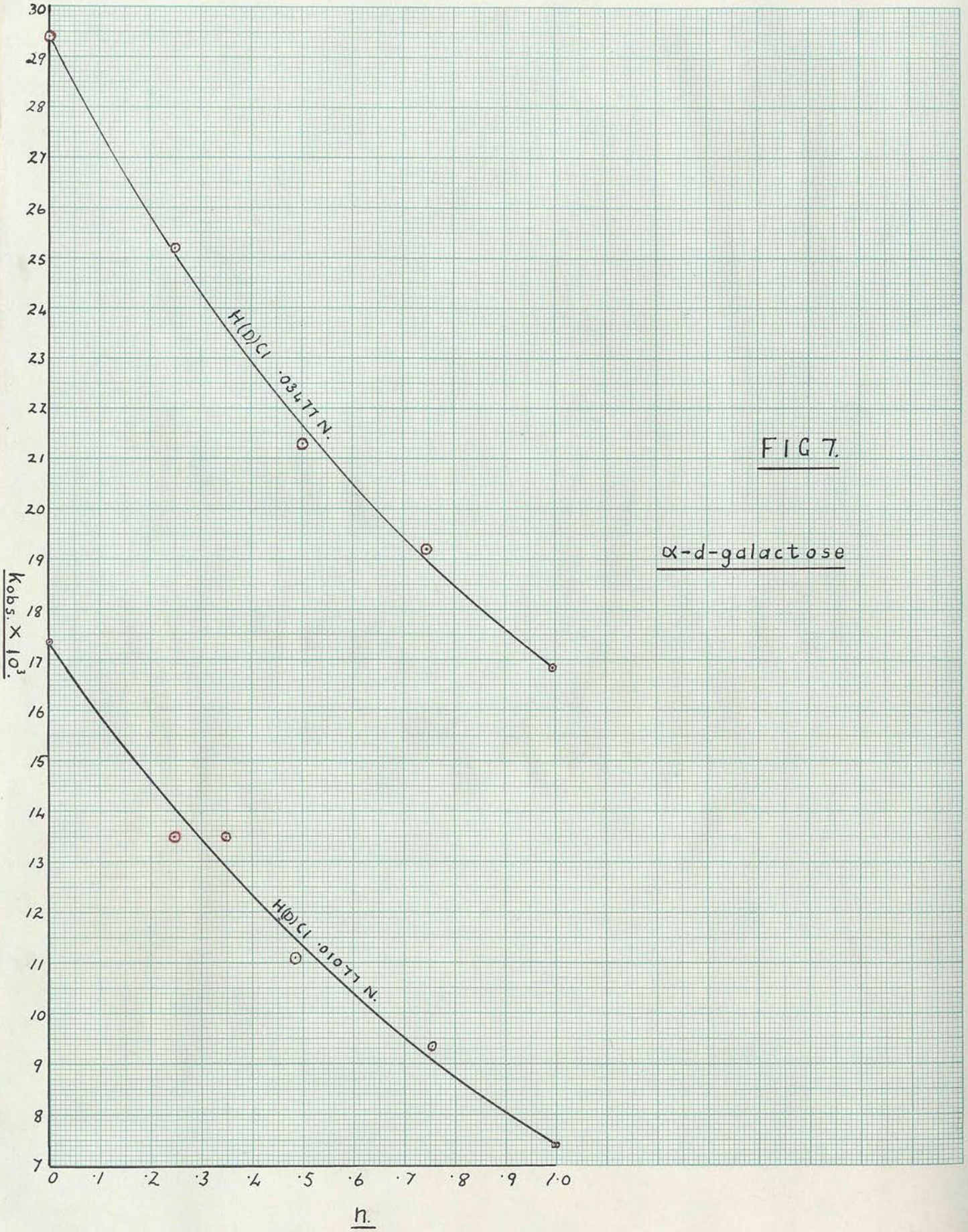


FIG 7.

α-d-galactose

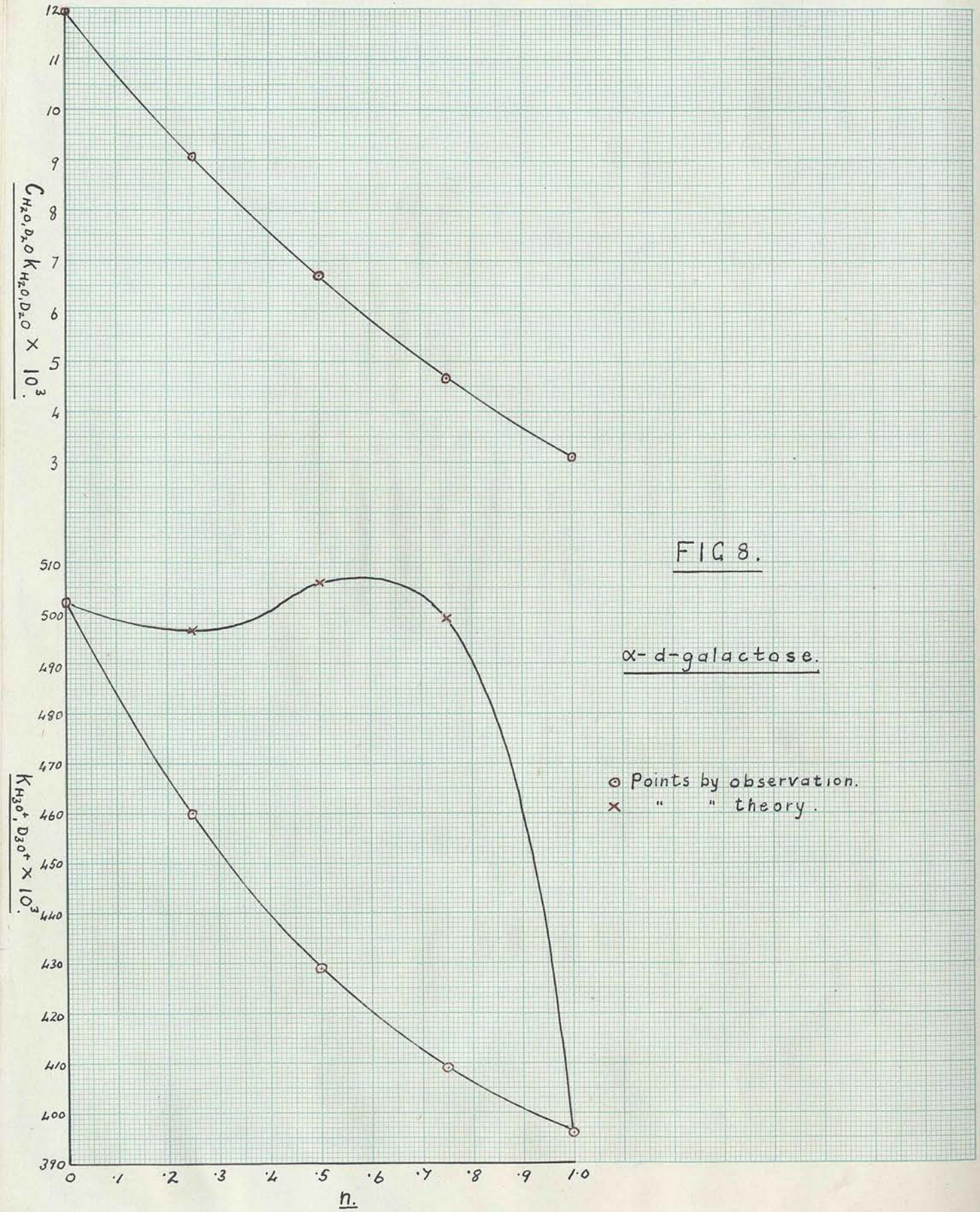


FIG 8.

α-d-galactose.

⊙ Points by observation.
× " " theory.

Table 9 below shows the mutarotation velocities obtained for isotopic mixtures in ·03477 N H(D)Cl solutions.

Table 9.

Atom fraction D in solvent = n.	Observed velocity constant. $k_{obs.} \times 10^3$
0·000	28·9, 29·4, 29·8, Aver. = 29·4
0·249	25·2
0·501	21·3
0·747	19·2
0·995	16·8, 16·9 Aver. = 16·9
1·000	16·8 By extrapolation.

The other conditions and procedure are the same as for the experiments in ·01077 N H(D)Cl solutions.

The data of tables 7 and 9 is shown in Fig. 7. Table 10 and Fig. 8 show the values of $k_{H_3O^+D_3O^+}$ and $C_{H_2O,D_2O}k_{H_2O,D_2O}$ derived using equations (11) or (12).

Table 10.

Ratio $\frac{D}{D + H}$ in solvent.	$k_{H_3O^+D_3O^+} \times 10^3$	$C_{H_2O,D_2O}k_{H_2O,D_2O} \times 10^3$
0·00	502	11·94
0·25	460	9·07
0·50	429	6·70
0·75	409	4·67
1·00	396	3·11

From the values obtained the ratios of the constants in pure light water to those in pure heavy water are,

$$\frac{k_{H_3O^+}}{k_{D_3O^+}} = 1{\cdot}27 \quad ; \quad \frac{k_{H_2O}}{k_{D_2O}} = 3{\cdot}84$$

The velocity constant of light water, $C_{H_2O,D_2O}k_{H_2O,D_2O} \times 10^3$, obtained by the above method is 11·9 and agrees with the value obtained directly, 11·7; see Fig.6.

In deriving the ratio $\frac{D}{D + H}$ for the solvent it has been assumed that no exchange occurs between the H-atoms of the sugar and the D-atoms of the solvent. In any case if exchange occurred at all at the OH-groups of the sugar there is involved at most an error of one per cent in the ratio and this is not greater than the experimental error in deriving the velocity constants.

Catalysis by Hydroxyl and Deuteroxyl Ions.

By working on the alkaline side of the mutarotation velocity-pH curve it was thought that the catalytic constants of the ions -OH and -OD could be found. Buffer solutions containing equal molar quantities of primary potassium phosphate, KH_2PO_4, and secondary sodium phosphate, NaH_2PO_4, were prepared in light and heavy water. The same quantities of sugar and solvent were used and the same procedure adopted as for the previous mutarotation experiments. The results are shown in Table 11.

Molarity of buffers with respect to either KH_2PO_4 or Na_2HPO_4 = ·01581

Ionic strength of solutions = ·063

Temperature = 15±·05°C.

Table 11

Buffer solvent	$k_{obs.} \times 10^3$
Light water	43·3
Heavy water	14·3

For mutarotation in alkaline solution equations (11) and (12), for observations in pure light and pure heavy water respectively, reduce to,

$$k_{obs.H_2O} = C_{H_2O}k_{H_2O} + [OH^-]k_{OH^-} \quad (13)$$

$$k_{obs.D_2O} = C_{D_2O}k_{D_2O} + [OD^-]k_{OD^-} \quad (14)$$

since the catalytic activities of the H_3O^+ and D_3O^+ ions are negligible. To find k_{OH^-} and k_{OD^-} the concentrations of the hydroxyl and deuteroxyl ions must be calculated. From the extended Henderson equation,

$$pH = pK_{2,H_2O} + \log\frac{[Na_2HPO_4]}{[KH_2PO_4]} - 1\cdot5\sqrt{\mu} + C\mu \quad (15)$$

$$pD = pK_{2,D_2O} + \log\frac{[Na_2HPO_4]}{[KH_2PO_4]} - 1\cdot5\sqrt{\mu} + C\mu \quad (16)$$

which fix the H_3O^+ and D_3O^+ concentrations in the buffer solutions.

μ = ionic strength of solutions.

K_2 = second dissociation constant of H_3PO_4, i.e., constant for process, $H_2PO_4^- \rightleftharpoons H^+ + HPO_4^=$

Recent measurements by Schwarzenbach, Epprecht, and Erlenmeyer[25] using the deuterium electrode show that $pK_{2H_2O} = 7{\cdot}207$; $pK_{2D_2O} = 7{\cdot}666$ at 20°C. For the solutions used therefore,

$$pH = 7{\cdot}207 \qquad pD = 7{\cdot}666$$

neglecting for the moment the ionic terms.

To obtain the OH^- and OD^- concentrations Wynne-Jones' values for the ionic products of light and heavy water were used.[18]

$$\text{i.e., } [H^+][OH^-] = 10^{-14{\cdot}35} \; ; \; [D^+][OD^-] = 10^{-15{\cdot}08}$$

at 15°C. and zero ionic strength. The concentrations are expressed in moles per litre.

Thus for the above solutions,

$$[OH^-] = 10^{-7{\cdot}143} \; ; \; [OD^-] = 10^{-7{\cdot}414}$$

From equations (13) and (14) by substitution, we have

$$43{\cdot}3 = 11{\cdot}9 + 10^{-7{\cdot}143}.k_{OH^-} \therefore k_{OH^-} = 4{\cdot}364 \times 10^8$$

$$14{\cdot}3 = 3{\cdot}1 + 10^{-7{\cdot}414}.k_{OD^-} \therefore k_{OD^-} = 2{\cdot}906 \times 10^8$$

$$\therefore \frac{k_{OH^-}}{k_{OD^-}} = 1{\cdot}50$$

To take into account the ionic terms in equations (15) and (16) changes the actual values of k_{OH^-} and k_{OD^-} somewhat but causes a negligible change in the ratio of the two. The catalytic effect of the other

anions present in the solution have been assumed to cancel out in the ratio. Another source of error lies in the evaluation of pH and pD since the values of pK_{2,H_2O} and pK_{2,D_2O} are obtained from Schwarzenbach's data for 20°C. while the above experiments were carried out at 15°C. The error involved here is unknown since we have no knowledge of the temperature coefficients of the dissociation constants involved.

DISCUSSION

It has been shown in the introduction that the use of deuterium compounds has provided a means of distinguishing in suitable cases the various mechanisms of acid - or base - catalysed reactions.

Hydrolysis of Ethyl Formate and Methyl Acetate.

Dawson[26] has found that in the case of simple esters, e.g., methyl acetate, general catalysis by undissociated acid molecules and anions is shown besides the catalysis due to the ions of water. In the case of ethyl acetate in acetic acid - sodium acetate mixtures the observed velocity constant is shown to be the sum of the individual constants due to the different ions and molecules. When acetic acid is used in absence of the corresponding salt the terms due to the undissociated molecule and the acetate-ion are very small and can in general be neglected in comparison with the hydrogen ion effect. When hydrochloric acid is used as catalyst the effect of introducing these terms is even smaller, in dilute solution. In solutions more concentrated than ·2 molar the effect of the undissociated acid on the catalysis may not be negligible and quite possibly 'undissociated' hydrochloric acid is a very effective catalyst[27].

For these esters there does not appear to be any possibility of a preequilibrium followed by general

basic catalysis as in the case of enolisation of acetone (see p.4). This can be seen if we assume the following reaction scheme,

a) $R_1.C(=O)OR_2 + H_3O^+ \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \left[R_1.C(=O).O(H).R_2\right]^+ + H_2O$ (equilibrium)

b) $\left[R_1.C(=O).O(H).R_2\right]^+ + H_2O \xrightarrow{k_3} R_1.C(=O).O(H) + \left[H.O(H).R_2\right]^+$ (slow)

c) $\left[R_2.O(H).H\right]^+ + H_2O \rightleftharpoons R_2OH + H_3O^+$ (equilibrium)

Thus a comparison of the K_n vs. n curve obtained from experiment with that derived theoretically should give conclusive evidence as to the existence of general acid catalysis.

Referring to page 10 the following equation was derived,

$$\xi_n = \frac{1}{Q'(n)}\left\{(1 - n)\phi(1 - n) + \frac{K_1}{K_o}Q'(1)n\phi(n)\right\}$$

$Q'(n)$ has already been derived theoretically and knowing $\frac{K_1}{K_o}$ from experiment the theoretical values of ξ_n for varying isotopic mixtures can be calculated. This has been done for ethyl formate and methyl acetate and the results are shown in Tables 12 and 13.

Ethyl Formate.

Table 12

$$\frac{K_1}{K_o} = \frac{20{\cdot}15}{14{\cdot}70} = \xi_{(1)} = 1{\cdot}37.$$

n	ξ_n calculated	$K_n \times 10^3$ calculated
0·00	1·00	14·7
0·25	1·04	$15{\cdot}2_8$
0·50	$1{\cdot}13_1$	$16{\cdot}6_2$
0·75	$1{\cdot}26_3$	$18{\cdot}5_8$
1·00	$1{\cdot}37_1$	$20{\cdot}1_5$

Methyl Acetate.

Table 13

$$\frac{K_1}{K_o} = 1{\cdot}60 \quad ; \quad K_o = K_{H_3O^+} = 3{\cdot}87 \times 10^3$$

n	ξ_n calculated	$K_n \times 10^3$ calculated
0·00	1·00	3·87
0·25	1·06	4·10
0·50	1·18	4·56
0·75	1·37	5·31
1·00	1·60	6·20

The calculated velocity constants for the above two reactions have been entered in Figs. 3 and 4 respectively to give a comparison with the observed values.

For ethyl formate there is agreement between

observed and calculated constants within the experimental error which admittedly is fairly high since difficulty was experienced in obtaining satisfactory end-points by the interferometer method.

For the methyl acetate reaction the calculated and observed values for the velocity constants are in fairly close agreement.

It must be concluded therefore that in the case of hydrolysis of those simple esters the complex is in thermodynamic equilibrium with the medium and general catalysis by acids is improbable.

It has recently been pointed out by Bonhoeffer and Reitz[4] that the function Q'(n) obtained from equation (8) i.e.,

$$Q'(n) = \frac{1}{\xi_n}\left\{(1 - n)\phi(1 - n) + \frac{K_1}{K_0} Q'(1)n\phi(n)\right\}$$

can be derived on certain assumptions without necessarily assuming a preequilibrium between proton and substrate. Also if the values computed for Q'(n) from kinetic and thermodynamic data do not agree, it is shown that agreement may be reached by considering the different velocities with which the complex finally reacts with H_2O, HDO and D_2O, i.e., the dependence of k_3 of equation (5) on the medium. Either of two assumptions can then be made both of which lead to a different form of the function Q'(n) including terms additional to those in equation (8). Gross, Steiner & Krauss[28] attempted to account for the

deviations met with in the inversion of cane sugar by considering these additional terms but on no account could the kinetic and thermodynamic functions be harmonized. They therefore conclude that the objections of Bonhoeffer and Reitz to comparing of kinetic and thermodynamic data is not justified. The latter assume as the criterion of preequilibrium in acid-catalysed reactions that the reaction rate is greater in heavy than in light water.

Decomposition of Diacetonealcohol.

From equation (9) on page 16 i.e.,

$$\frac{K_n}{K_o} = \xi_{(n)} = \left\{\frac{1 + \xi_{(1)}R(n)}{1 + R(n)}\right\}$$

the values for the velocity constants of the decomposition for various isotopic concentrations can be calculated the assumption being that the reaction velocity is proportional to the combined activities of the ions ^-OH and ^-OD. Table 14 gives the results of the calculation.

Table 14

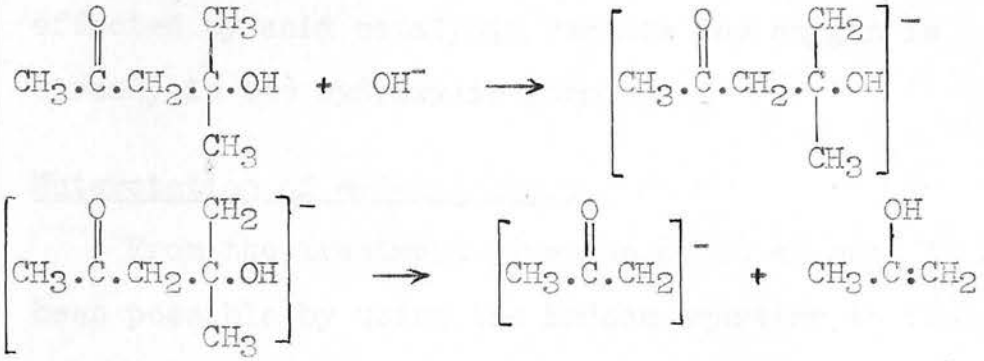
$\xi_{(1)} = \frac{K_1}{K_o} =$ 1·45 from data on p. 35.

n	$\xi_{(n)}$	$K_n \times 10^3$
0·00	1·000	19·8
0·25	1·091	21·6
0·50	1·188	$23·5_2$
0·75	1·302	25·8
1·00	1·450	28·7

Fig. 5 gives a comparison of the calculated with the observed values of the constants.

The observed rate is practically linear with the D-content of the solvent while the calculated curve Kn vs. n has a slight but definite sag.

The discrepancy between the two curves favours the view that the reaction does not proceed by way of an equilibrium but the difference is too small to be conclusive. More definite evidence for the mechanism however is obtained from the decomposition of the 'heavy' compound (see p.36). Both in heavy and in light water the 'heavy' compound reacts appreciably more slowly than the 'light' compound for solutions of the same alkalinity. This difference in velocity is greater than can be explained by the increased mass and consequently smaller collision number of the 'heavy' compound. The difference between the reaction rate for the 'light' compound and that for the 'heavy' should be considerably greater if diacetonealcohol of 100% atom-D were used instead of the compound of 60·4% atom-D which was actually used in the experiments. Thus it would appear that the rate-determining step in the reaction is a proton or deuteron transfer from the compound to the ^-OH or ^-OD ion and the following mechanism is indicated.



The proton would most naturally be lost from one of the terminal methyl groups adjacent to the hydroxylic oxygen atom. This would convert that half of the molecule into a enolic acetone and the molecule would then split up into an enolic acetone and the corresponding ion.

The above mechanism accounts for all the main features of the reaction.

(1) The 'heavy' alcohol reacts more slowly than the light because the transfer of D^+ from the compound to the -OH and -OD ions is slower than the corresponding transfer of H^+.

(2) The 'light' alcohol reacts more quickly in heavy water than in light because the rate of transfer of a proton to the deuteroxyl ion in heavy water is more rapid than to a hydroxyl ion in light water. Incidentally the ratio of the rates of the two processes, in the above case 1·45, agrees well with the same ratio obtained in the case of neutralisation of nitroethane (equations (1) and (2)).

(3) The reaction is not catalysed by acids. The enolisation of the terminal acetone cannot be

effected by acid catalysis because the oxygen is already in the hydroxylic form.

Mutarotation of ∝-d-galactose.

From the treatment given on p. 40 et seq. it has been possible by using the Hudson equation to isolate the catalytic constants for the water molecules and for the hydrogen ions in isotopic water mixtures of constant acidity. When $k_{H_3O} + D_{3O^+}$ is plotted against n (Fig. 8) a sagged curve is obtained contrary to the findings of Hamill and La Mer who obtained a straight line for the analogous case of ∝-d-glucose at 25°C. For catalysis by the molecules of water, however, k_{H_2O,D_2O} vs. n (Fig. 8) yields a sagged curve similar to that obtained for glucose by these authors.

From equation (8), i.e.

$$Q'(n) = \frac{1}{5^n}\left\{(1 - n)\phi(1 - n) + \frac{K_1}{K_o}Q'(1)\, n\, \phi(n)\right\}$$

it is possible to calculate the catalytic constants for the hydrogen-ion catalysed reaction for various isotopic mixtures on the assumption, as before, that the reaction rate is proportional to the activities of protons and deuterons. The results are shown in Table 15.

Table 15

$$\xi_{(1)} = \frac{K_1}{K_0} = \frac{396 \times 10^3}{502 \times 10^3} = .788 \text{ from data on p.41.}$$

n	$\xi_{(n)}$	$K_n \times 10^3 = k_{H_3O^+D_3O^+} \times 10^3$
0·00	1·000	502·0
0·25	0·990	496·5
0·50	1·007	506·0
0·75	0·993	499·0
1·00	0·788	396·0

The calculated constants for the hydrogen-ion catalysis are shown in Fig. 8 together with the observed constants. The two curves are entirely different in character. The theoretical curve is convex upwards and has one point of inflexion, while the observed curve is smooth with a downward sag. This result seems to indicate that the reaction does not proceed by way of a preequilibrium with the H_3O^+ and D_3O^+ ions and supports Bonhoeffer and Reitz' contention that the rate-determining step is a proton transfer, i.e., referring to equation 5, p. 3,

$$\text{Rate of reaction, } k = \frac{k_1 . k_3}{k_2 + k_3}$$

For mutarotation of galactose $k_2 \ll k_3$

$$\therefore \quad \underline{k = k_1}$$

For the case of a simple ester hydrolysis, however, $k_3 \ll k_2$.

$$\therefore \quad k = \frac{k_1}{k_2}.k_3 = Kk_3$$

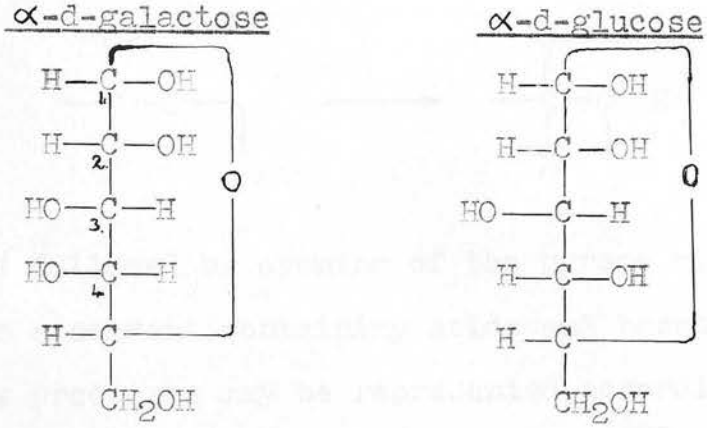
i.e., the rate is proportional to the concentration of the intermediate complex.

A comparison between the data for mutarotation of α-d-galactose obtained here and α-d-glucose obtained by other workers is made below in Table 16.

Table 16

	α-d-galactose	α-d-glucose
$\frac{k_{H_3O^+}}{k_{D_3O^+}}$	1·27 at 15°C.	1·78 at 14·80°C.[20] 1·37 " 25°C.[16]
$\frac{k_{H_2O}}{k_{D_2O}}$	3·84 " "	3·12 at 14·80°C.[20] 3·80 " 25°C.[16]
$\frac{k_{OH^-}}{k_{OD^-}}$	1·50 " "	
$\frac{k_{(CH_3COO^-)\text{in } H_2O}}{k_{(CH_3COO^-)\text{in } D_2O}}$	-	2·38 at 24.97°C.[16]
$\frac{k_{CH_3COOH}}{k_{CH_3COOD}}$	-	2·59 " " "

The similarity between the two sets of data is close and the slight differences should be accounted for by the temperature effect, which would alter the activation energy, combined with minor steric effects arising out of the different structures of the two sugars which are identical except for the grouping on the fourth carbon atom, i.e.,



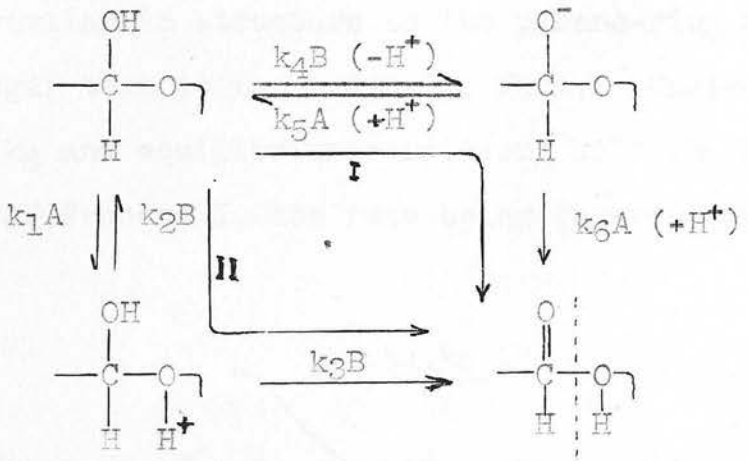
As mentioned on p.18, La Mer has suggested that the water-catalysed mutarotation of glucose can be explained on the assumption that exchange between solvent and the aldehydic hydrogen of the glucose takes place rapidly and that the reaction rate then varies linearly with the proportion of this 'heavy' glucose in the solution, the solvent having no further influence on the rate. This is equivalent to saying that the change in velocity constant on going from light to heavy water is due only to variation of acidity of the substrate. Although La Mer's theory explains his own results for the water-catalysed mutarotation of glucose the actual mechanism of the mutarotation is undoubtedly more complicated than is

implied in the above scheme.

Mutarotation is essentially a prototropic isomerization, i.e., a reaction involving the change of position in the molecule of a proton with, usually, a rearrangement of bonds. In the case of the hexoses, e.g., glucose and galactose, the reaction may be represented by the following scheme.

This is followed by opening of the pyrane ring.

In a solvent containing acids and bases, the various processes may be represented, according to Pedersen's scheme of prototropic changes[29], by the following.



A and B denote the concentration of the acid or base respectively.

Process I is a basic followed by an acid catalysis

while Process II is the reverse. In an acid-base medium the observed velocity will be the sum of the velocities of Processes I and II since the final result can be attained by either. If their respective rates are v_1 and v_2 we have,

$$v_1 = \frac{k_6 A . k_4 B}{(k_5 + k_6)A} = \left(\frac{k_4 . k_6}{k_5 + k_6}\right) B$$

$$v_2 = \frac{k_1 . k_3 . A . B .}{(k_2 + k_3)B} = \left(\frac{k_1 . k_3}{k_2 + k_3}\right) . A$$

Thus Process I appears to be catalysed by bases in general and Process II by acids in general.

Which of the two stages of Process I is likely to determine the rate depends on the similarity in electronic structure of the intermediate ion to the initial or final form of the sugar. For glucose and galactose it is probable that the intermediate ion is more similar in structure to the pyrane-ring form of the sugar than to the aldehydic form. Consequently $k_5 \gg k_6$ and equilibrium conditions hold in the first stage of Process I, the rate being governed by k_6. Hence,

$$v_1 = \frac{k_4 . k_6}{k_5} . B$$

Similarly for Process II $k_2 \gg k_3$ and,

$$v_2 = \frac{k_1 . k_3}{k_2} . A$$

Generally for any acid, HA say, in presence of water which can act both as acid and base we have the

following three acid-base pairs.

Base	Acid
H_2O	H_3O^+
OH^-	H_2O
A^-	HA

which each give a different value of k_1, k_2 etc. It may be noted here, however, that H_2O is probably much more of a basic than an acid catalyst.

For the observed velocity of mutarotation in such a system we have,

$$v_1 + v_2 = \frac{k_4 . k_6}{k_5} . H_2O + \frac{k_1 . k_3}{k_2} . H_3O^+ + \frac{k_4' . k_6'}{k_5'} . OH^-$$

$$+ \frac{k_1' . k_3'}{k_2'} . H_2O + \frac{k_4'' . k_6''}{k_5''} . A^- + \frac{k_1'' . k_3''}{k_2''} . HA$$

This expression can be put in a more convenient form by introducing the following equilibrium constants.

$$K_{(GH)_1} = \frac{G^- . H_3O^+}{GH . H_2O} \quad ; \quad K_{(GH)_2} = \frac{GH_2^+ . H_2O}{GH . H_3O^+}$$

where,

GH = concentration of initial form of sugar.

G^- = " " intermediate ion in Process I .

GH_2^+ = " " " " " " II.

The above expression then reduces to,

$$v_1 + v_2 = K_{(GH)_1} \left\{ k_6 H_2O + \frac{k_6'}{K_W} . OH^- + \frac{k_6''}{K_A} . A^- \right\}$$

$$+ K_{(GH)_2} \left\{ k_3 . H_3O^+ + k_3' . H_2O . K_W + k_3'' . K_A . HA \right\} \qquad (17)$$

where K_w = water constant, $[H^+][OH^-]$.

K_A = dissociation constant of HA.

Hamill and La Mer[16] have examined the effect of substitution of H_2O by D_2O on the Brönsted equations in the case of mutarotation of glucose. For bases the Brönsted relation is,

$$k_B = G_B.K_B^{\ y}$$

where k_B = velocity constant for catalysis by base. G_B and y are constants for the base-catalysed reaction in a given solvent.

K_B = dissociation constant of base.

For acids the corresponding relation is,

$$k_A = G_A.K_A^{\ x}$$

Here the constants G_A and x are different from those of the base-catalysed reaction.

The constants of the Brönsted equations were obtained by substitution in the above equations of the known data for the bases H_2O, D_2O, and acetate ion in light and heavy water, and for the conjugate acids H_3O^+, D_3O^+ and acetic acid in light and heavy water. The results are shown in Table 17 below.

Table 17

Base	G_B	y
H_2O	$8{\cdot}7(10)^{-4}$	0·384
$Ac^-(H_2O)$		
D_2O	$2{\cdot}3(10)^{-4}$	0·382
$Ac^-(D_2O)$		

Acid	G_A	x
H_3O^+	0·11	0·27
HAc		
D_3O^+	0·07	0·29
DAc		

It is seen that the constants x and y are not affected very much by the medium H_2O or D_2O. Thus for the ratio of the G's,

$$\frac{G_{H_2O}}{G_{D_2O}} = \frac{k_{oH_2O}}{k_{oD_2O}}$$ for base catalysis,

where $k_{oH_2O} = 55\ k_{H_2O}$ and $k_{oD_2O} = 55\ k_{D_2O}$

and $\frac{G_{H_2O}}{G_{D_2O}} = \frac{k_{H_3O^+}}{k_{D_3O^+}}$ for acid catalysis, the subscript H_2O and D_2O referring to conditions in light and heavy water respectively.

We can write,

$$\frac{k_{B,H_2O}}{k_{B,D_2O}} = 3{\cdot}8 \left[\frac{K_{B,H_2O}}{K_{B,D_2O}}\right]^y = 3{\cdot}8 \left[\frac{K_{A,D_2O}}{K_{A,H_2O}}\right]^y$$

for glucose mutarotation.

$$\frac{k_{A,H_2O}}{k_{A,D_2O}} = 1{\cdot}37 \left[\frac{K_{A,H_2O}}{K_{A,D_2O}}\right]^{x}$$

For hydrogen ion the ratio $\frac{K_{A,D_2O}}{K_{A,H_2O}}$ is a maximum at a value 1, and for H_2O this ratio shows a minimum with a value of $\frac{1}{6}$. Thus it would seem that,

$\frac{k_{B,H_2O}}{k_{B,D_2O}}$ is a maximum when the base, B, is H_2O and D_2O, and

$\frac{k_{A,H_2O}}{k_{A,D_2O}}$ is a minimum when A = H_3O^+, D_3O^+.

For galactose and glucose the experimental data confirm the above argument. The measured water rate is probably mainly that of water as a basic catalyst and the ratio k_{H_2O}/k_{D_2O} is considerably greater than that of k_{OH^-}/k_{OD^-}. Thus for galactose (see Table 16),

$$\frac{k_{H_2O}}{k_{D_2O}} = 3{\cdot}84 \; ; \quad \frac{k_{OH^-}}{k_{OD^-}} = 1{\cdot}50 \text{ at } 15^{\circ}C.$$

We can proceed further in the analysis of the constants on the basis of the above scheme.

(1) For acid catalysis,

$$\frac{k_{A,H_2O}}{k_{A,D_2O}} = \frac{K_{(GH)_2}}{K_{(GD)_2}} \cdot \frac{k_{3,H_2O}}{k_{3,D_2O}} \cdot \frac{K_{A,H_2O}}{K_{A,D_2O}}$$

where $K_{(GH)_2}$ is as on p. 59 and $K_{(GD)_2} = \frac{GHD^+ . D_2O}{GH . D_3O^+}$.

K_{A,H_2O} and K_{A,D_2O} are the dissociation constants of the

acids in H_2O and D_2O respectively.

If the acid is H_3O^+, D_3O^+ $\therefore K_{A,H_2O} = K_{A,D_2O}$

$$\therefore \frac{k_{A,H_2O}}{k_{A,D_2O}} = \frac{K_{(GH)_2}}{K_{(GD)_2}} \cdot \frac{k_{3,H_2O}}{k_{3,D_2O}}$$

$$= 1{\cdot}37 \text{ for glucose at } 25^\circ C.$$

$$\text{or} = 1{\cdot}27 \text{ " galactose at } 15^\circ C.$$

From analogy with the simple ester catalysis the concentration of the D-complex in such a case as the above is greater than that of the H-complex, i.e.,

$$K_{(GD)_2} > K_{(GH)_2}$$

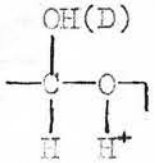
The constants k_3 refer to the second stage of Process II in the scheme given on p. 57, i.e.,

$$\left.\begin{matrix} GH_2^+ \\ GHD^+ \end{matrix}\right\} + \text{base} \xrightarrow{k_3 B} \begin{matrix} (GH + \text{acid} & (a) \\ (& \\ (GH + \text{acid} & (b). \end{matrix}$$

This involves a proton or deuteron transfer from the intermediate ion to the base. The rate of transfer of a proton to the base, which takes place in light water, reaction (a), is greater than the rate of transfer of a deuteron to the base which takes place in heavy water, reaction (b). These stages may be compared to the solvent decomposition of nitramide, a base-catalysed reaction, examined in isotopic water by La Mer and co-workers[30]. In this case it would seem to be possible to obtain the relative rates of proton and deuteron transfer from light and heavy nitramide respectively, to the base water, but since a practically instantaneous

exchange occurs between the H atoms of the $-NH_2$ group of the nitramide, and the heavy water, a comparison can only be made of the rate of uptake of D^+ to D_2O and H^+ to H_2O. Neglecting this exchange effect the ratio $\frac{k \text{ proton-transfer}}{k \text{ deuteron }"}$ for nitramide decomposition is found to be 6. It is thus possible to understand why essentially smaller ratios of $k_{A,H_2O}/k_{A,D_2O}$ are obtained in this case than in reactions involving proton transfers without previous formation of a complex ion.

La Mer's treatment of the variation of the rate with the D-content deals essentially with $k_{3,H_2O}/k_{3,D_2O}$. This ratio is determined by,

(a) The fraction of deuterium in the -OH group, whose H atom exchanges rapidly, i.e., 

This fraction is determined by the exchange,

$$GH + HDO \rightleftharpoons GD + H_2O.$$

(b) The basic nature of the medium. If the base is the water molecule, we can have three species, H_2O, HDO, D_2O, each with their own proton-accepting capacity.

The rate would then be given by the following,

$$\text{Rate} = \left\{k_{H_2O}\left[1 + (k_{D_2O} - k_{H_2O})F_{DG}\right]\right\}(k_1 C_{H_2O} + k_2 C_{HDO} + k_3 C_{D_2O})$$

where the first factor on the right-hand side accounts for variation of acidity of the substrate molecule while the second accounts for variation of basicity of

the medium. It must be noted here that the constants k_1, k_2 etc., in the above expression have not the same significance as hitherto but denote the rate of proton or deuteron transfer to the molecules H_2O, HDO, etc., where C_{H_2O}, C_{HDO} etc., are the respective concentrations.

To obtain the observed rate the above expression would have to be multiplied by a quantity representing the concentration of the complex ion in the given medium. The formation of the two ions, i.e.,

$GH + H^+ \rightleftharpoons GH_2^+$ (a) Equilibrium constant, K_H^+.

$GH + D^+ \rightleftharpoons GHD^+$ (b) " " , K_D^+.

depends on the proton and deuteron activities in the solution. From the treatment given on p. 7 et seq. we have, for the concentration of those ions,

$$GH_2^+ = K_{H^+}.GH.\alpha_{H^+} = K_{H^+}.GH.\frac{[H_2O]^{\frac{1}{2}} f^+_{\Sigma H_3O^+}}{Q'(n)}$$

$$GHD^+ = K_{D^+}.GH.\frac{[D_2O]^{\frac{1}{2}} f^+_{\Sigma H_3O^+}}{Q'(n).\sqrt{L}}$$

Thus the total concentration of the complex ions is,

$$GH\left[\frac{K_{H^+}[H_2O]^{\frac{1}{2}}}{Q'(n)} + \frac{K_{D^+}[D_2O]^{\frac{1}{2}}}{Q'(n)\sqrt{L}}\right] f^+_{\Sigma H_3O^-}$$

The combined effect of all those factors results in a complex expression for the rate in a given medium and since there are so many constants it is very difficult to calculate the form of the curve $k_{obs.}$ vs. n.

(2) For basic catalysis we have for the relative rates,

$$\frac{k_{B,H_2O}}{k_{B,D_2O}} = \frac{K_{(GH)_1}}{K_{(GD)_1}} \cdot \frac{k_{6,H_2O}}{k_{6,D_2O}} \cdot \frac{K_{B,H_2O}}{K_{B,D_2O}}$$

where, $K_{(GD)_1} = \frac{G^-.D_3O^+}{GD.D_2O}$ and K_{B,H_2O} and K_{B,D_2O} are the dissociation constants of the base in H_2O and D_2O respectively.

For water as a basic catalyst K_{B,H_2O} is equal to K_{B,D_2O} by definition and the last ratio in the above expression disappears. Also since galactose and glucose are weak acids we can almost certainly put,

$$K_{(GH)1} > K_{(GD)_1} \quad \therefore \quad \frac{K_{(GH)_1}}{K_{(GD)_1}} > 1$$

The constants k_{6,H_2O} and k_{6,D_2O} refer to acid catalysis, in the second stage of Process I, by H_3O^+ and D_3O^+ respectively. Since H_3O^+ is a stronger acid than D_3O^+,

$$\frac{k_{6,H_2O}}{k_{6,D_2O}} > 1$$

Thus for water the ratio $\frac{k_{B,H_2O}}{k_{B,D_2O}}$ is the product of two ratios both greater than unity. From the data,

$\frac{k_{B,H_2O}}{k_{B,D_2O}}$ = 3·80 for glucose at 25°C.

and = 3·84 " galactose " 15°C.

For the ions OH^- and OD^- as catalysts the additional ratio $\frac{K_{B,H_2O}}{K_{B,D_2O}}$ has to be taken into account. In this case we know that,

$$K_{B,H_2O} < K_{B,D_2O} \quad \therefore \quad \frac{K_{B,H_2O}}{K_{B,D_2O}} < 1$$

although $\frac{k_{6,H_2O}}{k_{6,D_2O}}$ is still greater than unity. This reduces the ratio $\frac{k_{B,H_2O}}{k_{B,D_2O}}$ and,

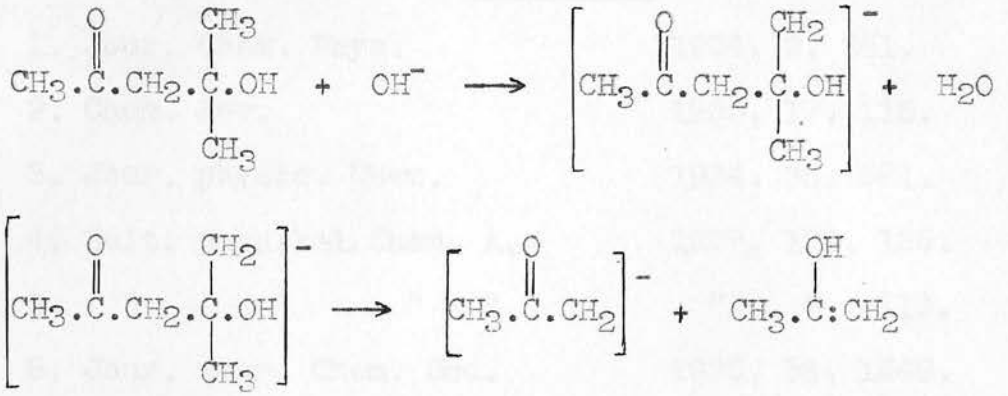
$$\frac{k_{B,H_2O}}{k_{B,D_2O}} = 1{\cdot}5 \text{ for galactose at } 15^{\circ}C.$$

To conclude it may be pointed out that if the ratios $\frac{K_{(GH)_1}}{K_{(GD)_1}}$ and $\frac{K_{(GH)_2}}{K_{(GD)_2}}$ were known for the base-catalysed and acid-catalysed reaction respectively it would be possible to determine what part of the total ratio $\frac{k_{B,H_2O}}{k_{B,D_2O}}$ or $\frac{k_{A,H_2O}}{k_{A,D_2O}}$ is due to the relative equilibrium constants and what to the relative values of k_6 or k_3. The ratio $\frac{K_{(GH)_1}}{K_{(GD)_1}}$ could be found by measuring the relative dissociation constants of the sugar in light and heavy water but $\frac{K_{(GH)_2}}{K_{(GD)_2}}$ is not directly accessible. Further investigation is therefore necessary to find the velocity constants involved in the different stages of the mutarotation.

SUMMARY

1. The rates of the acid-catalysed hydrolyses of ethyl formate and methyl acetate in mixtures of light and heavy water have been found. In both cases the variation of the rate with the D-content of the medium gives a sagged curve which agrees within the experimental error with the thermodynamic curve calculated on the assumption of an equilibrium between the substrate, the intermediate complex, and the hydrogen ions. The reactions are therefore not cases of general acid catalysis.

2. For the alkaline decomposition of diacetonealcohol in isotopic water mixtures the reaction rate is found to be practically linear with the D-content of the medium. The values deviate slightly but definitely from the thermodynamic curve which has been calculated for the alkaline reaction on the assumption of an equilibrium between the ions OH^- and OD^- and the substrate. Similar experiments with 'heavy' diacetonealcohol, for which a decrease in reaction rate is found in all media, show that the rate-determining step is the transfer of a proton from the alcohol to the ion OH^- (or OD^-) according to the following.



3. The mutarotation of ∝-d-galactose in isotopic water mixtures has been examined and the relative rates of the catalysis by the ions H_3O^+, D_3O^+, OH^- and OD^-, and the molecules H_2O and D_2O have been found. The ratios agree well with the data obtained by Hamill and La Mer for the analogous case of ∝-d-glucose. The mechanism of the mutarotation process is discussed on the basis of Pedersen's scheme of acid-base equilibria in prototropic systems and an explanation is given of the difference in value of the above ratios in this case and in other cases involving proton and deuteron transfers.

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